



# EPIDEMICS AND CROWD- DISEASES

*An Introduction to the Study of Epidemiology*

by

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## PREFACE

THIS book is based on the instruction I give to professional students at the London School of Hygiene and Tropical Medicine, and will, I hope, be useful to them and to members of the public health services; but it is not a textbook prepared with an eye to an examination syllabus. I have tried to cater for a wider circle of readers than present or future members of the public health services, viz. *all* educated men and women interested in the communal aspects of health and disease. The demands made on the technical equipment of the reader are slight; at the worst, a student who has not been bred to medicine may find it helpful to turn up in an encyclopaedia or an ordinary textbook the clinical descriptions of the special diseases studied, the signs and symptoms. I think if one has some picture in one's mind of what is happening to the individuals of the group the story becomes more interesting. Educated people who are not "doctors" seem to me what Count Fosco said all Englishmen were, cautious in the wrong place. They are very ready to criticize the treatment of a patient in a particular case, equally ready to accept medical generalizations without criticism. But the opinion of a layman on particular diagnosis or treatment is usually worthless, for the layman has no experience to guide him, no skill in the differentiation of one set of circumstances from another. On the other hand, a man highly skilled in individual diagnosis and treatment may be quite unskilled in generalization. In this branch of medicine the work which no layman can usefully criticize is assumed to have been done before we begin. It is supposed that the people who were ill at Maidstone in 1897 really were suffering from typhoid fever, and that what interests us is how the things assumed to have happened did happen. The discussion of that problem needs logic and common sense, of which the medical profession has no monopoly.

A book written, as this has been, at odd moments and dealing, as this does, with many questions of which the writer has but second- or third-hand knowledge must contain many errors. I hope that such experts as do read it may temper justice with mercy in their judgments.

As R. L. Stevenson said, the reading of a classic, say the *Aeneid*, brings back to us not memories of old Italy but of our schooldays, of our fellow pupils and our teachers.

Even so, in preparing this book for the press, reading again the words of the heroes of old days or of great men still living or recently living, I am conscious of an aroma made up of memories from a recent past, *my* past, of the personalities of those who taught me. It is a pleasant but a deceptive atmosphere. It has perhaps led me to think that much which is intrinsically dull and unimportant is interesting and valuable.

The reader will form his opinion. If I have only persuaded him to study to better advantage some of the old books and dusty official reports which thrilled me, I shall not have wasted his time.

Many friends have helped me; I am particularly grateful to Dr. Bradford Hill for his criticism of the typescript and revision of the proofs.

MAJOR GREENWOOD

*November 1934*

# CONTENTS

<i>Preface</i>	<i>page</i> 9
----------------	---------------

## *Part I*

### *GENERAL PRINCIPLES AND METHODS*

I. Hippocrates and Galen	15
II. From the Revival of Learning to Graunt	31
III. Graunt and Afterwards	43
IV. The Age of Pasteur and Galton	58
V. Experimental Epidemiology	68
VI. The Artificial Immunization of Man	78
VII. Procatactic Causes—Nutrition	98
VIII. Procatactic Factors—Occupation	117
IX. Procatactic Factors—Psychological	127

## *Part II*

### *SPECIAL ILLUSTRATIONS*

I. The Typhoid Group	137
II. Cholera	165
III. Typhus	173
IV. Measles	180
V. Diphtheria	197
VI. Scarlet Fever	211
VII. Smallpox	226
VIII. Edward Jenner and Charles Creighton	245
IX. The Post-Jennerian Controversy	274

x.	Plague	<i>page</i> 289
xi.	Epidemic Diseases of the Central Nervous System	310
xii.	Influenza	320
xiii.	Venereal Diseases	331
xiv.	Tuberculosis	342
xv.	Cancer	361
	<i>Index</i>	379

*PART I*

GENERAL PRINCIPLES AND METHODS



## HIPPOCRATES AND GALEN

THE object of this book is to introduce a reader interested in some of the larger problems of preventive medicine to the methods of study which have been used and the results which have been attained. The problems I shall discuss have interested mankind for thousands of years, and a great variety of methods of solution has been proposed. In our own time it is believed that the most useful methods of study come under one or other of two technical expressions, Epidemiology and Vital Statistics, so that we shall best begin our task by inquiring what these terms mean.

Epidemiology suggests etymologically a science of something falling upon the people, and statistics suggests the study of states; as originally used the word statistics had no necessary connection with arithmetic. Epidemiology came to mean the study of disease, any disease, as a mass phenomenon. It differs from the study of disease by a clinician primarily in respect of the unit of investigation. A physician is concerned with, say, typhoid fever from the point of view of the individual patient, to determine from his experience and the results of his examination (a) that the patient is suffering from typhoid fever, (b) how the case is likely to develop—its prognosis, (c) what treatment is likely to give the patient the best chance of recovery.\* An epidemiologist is concerned with a prevalence of typhoid fever; he wishes to determine the probable course of that prevalence, whether there are likely to be more cases, when the maximum will be reached, what should be done to reduce the prevalence. The physician's unit of study is a single human being, the epidemiologist's unit is not a single human being but an aggregate of human beings, and since it is impossible to hold in the mind distinctly a mass of separate particulars he forms a general picture, an average of what is happening, and works upon that.

Statistics as a science may be defined in many ways; here is a

\* A *modern* physician will also, of course, give advice on how to limit the spreading of infection from his patient to others, but that is not his primary duty.

definition which I copied into my notebook more than twenty-five years ago. "The science of statistics is that which deals with distributed effects following a cause not uniquely determinative. The distributed results are spoken of as the variation due to this cause, and as a general rule we find the proportion of these effects, which remains sensibly constant if we take a large enough series of observations or experiments. This permanency of results will be spoken of as the Permanency of Statistical Ratios." I think this is a good definition, but as a very acute friend of mine told me that it had him beat perhaps an illustration will not be amiss. Whether a perfectly made penny shall fall head or tail uppermost depends on a great number of factors: on the force with which the thrower projects the coin, the angle of spin, the resistance of the air, and many other things. One might conceive of an art (or science) of individual coin-tossing diagnosis, some method which would enable us to tell from observation of the beginning of the process which way up the tossed coin would fall. If we saw that the tosser had the coin head upwards and threw it without spin (or dropped it with its surface parallel to the ground), then before the coin reached the ground we could accurately foretell the result. If, however, he did not let one see which side was uppermost, or spun the coin vigorously, prognosis would be *very* difficult; it would only be possible for a being with supernatural powers of observation. There is in fact no practicable art of individual coin-tossing prognosis. But if we abandon that problem, and ask ourselves not what will be the result of an individual throw but of sets of many throws, the position is different. The man in the street will tell you that, *in the long run*, head and tail fall equally often. He will agree that if you toss sets of ten coins there is likely to be a wider range of proportional variation from the "expected" result than if you had tossed sets of a thousand coins. The science of statistics enables us to give quantitative precision to these common-sense opinions. We can give reasonable rules of *group* prognosis in coin tossing, while *individual* prognoses are only guesses.

A reader will now see the connection between statistics so defined and epidemiology. In each individual "case" of typhoid fever there may be features different from those observed in any other case, but some common to a number of cases. Similarly,

there will be some characters of one *prevalence* which will liken it to another prevalence but distinguish it from a third. Thus a prevalence of typhoid conditioned by some pollution of a communal water supply, such an epidemic as that of Maidstone in 1897, presents in its evolution a more or less rapid increase to a maximum, and then a long decline not broken by notable irregularities; it falls into a group respecting which the epidemiologist—from a mere scrutiny of the statistics—may form a shrewd conjecture as to the main source of the prevalence, and the graph of a prevalence of this kind contrasts with the irregular zigzag time chart of a prevalence referable to carrier infection. In fact, with all the variation of individual factors the average type remains constant and diagnostic. Such a time chart of cases has the diagnostic value to the epidemiologist that the patient's temperature chart has to the clinician.

These reflections suggest that a statistical method is essential in the work of the epidemiologist, as essential as skill in manual diagnosis, in the use of clinical instruments, the stethoscope, the clinical thermometer, the sphygmomanometer is to the clinician. That suggestion has been accepted by a majority of medical men; but a respectable minority of epidemiologists, including men of great intelligence and wide experience, believe that the statistical method is of very small value to the practical epidemiologist and deprecate a dubious addition to the already heavy burden the medical post-graduate student is required to shoulder. Unless I can satisfy the reader that the view of the majority is correct, he will hardly turn over any more pages of this book, and I can only hope to satisfy him by describing the state of epidemiology prior to the introduction of the statistical method and by proving, or at least by trying to prove, that such defects as existed were indeed consequences of lack of the statistical method. On that account this and the next chapter will be mainly devoted to the history of epidemiology from remote times down to the end of the seventeenth century.

We shall not, however, look at medical history through the eyes of a specialist scholar. We will accept the simple and inaccurate formula that the science of medicine was founded in the age of Hippocrates, codified by Galen, revolutionized first in the seventeenth century by Harvey and Sydenham, then more completely

in the nineteenth century. We will only go into detail sufficiently to make plain how and where the quantitative method was concerned in the evolution of the science and art.

We begin with the age of Hippocrates.

The contribution of Hippocrates to clinical medicine cannot detain us; most readers know what it was, that he conceived ill-health as a process, essentially orderly, capable of being comprehended by the mind of man and accurately described in human language. He held, and proved, that upon the accurate observation of symptoms a rational method of prognosis could be based, and that by such a system rational indications for treatment could be derived. It is his greatness in this department that has mainly kept his memory green and led successive doctors, who were *primarily* healers of the sick, even when separated from him by hundreds of years—Galen in the second century, Sydenham in the seventeenth century, Osler in the twentieth century—all to speak of Hippocrates in nearly the same words. But although Hippocrates was before all else a clinician, he was also a student of preventive medicine and epidemiology, of the doctrine of disease as a mass phenomenon, the units not individuals but groups.

In the collections of writings known as the Hippocratic *corpus*, which existed in its present form long before the time of Galen, there are three treatises devoted to this branch of the profession, and these three treatises were accepted by the ancient writers and are still accepted by scholars as the work of one man and that man the physician whom Plato knew as Hippocrates. These books are the treatise on Airs, Waters, and Places, and the First and Third Books of Epidemics. All three may be read through in a few hours, all are available in accurate translation.

I will in a few sentences try to describe where Hippocrates stood. He recognized that some forms of sickness were always present in a population, but that other forms either were not usually present or, if present, were not common at all times, but became very frequent at certain periods of the year and in certain years. He distinguished, as we say—using words taken from him—between *endemic* and *epidemic* diseases. Further, he observed that the endemic diseases of different places were not the same. He then desired to solve two great problems:

- (1) What are the factors of local endemicity?
- (2) What are the reasons of epidemic prevalence?

The former problem is the subject of the *Airs, Waters, and Places*; the latter of the *Books of Epidemics*.

Already, three hundred and fifty years before Christ, a public health student was faced by quantitative problems, problems of the measurement of variable magnitudes. Hippocrates, therefore, approached them on quantitative lines. Having no statistics of variables of any kind, he visited the countries he wished to study and in the book mentioned we have his final judgments; he was a statistician in Achenwall's sense of the word. It is a book of observations and conclusions. In such-and-such a city the exposure is such-and-such, the drinking water is of such-and-such a quality, the prevailing winds are so-and-so. In this place such-and-such illnesses are endemic, the inhabitants are of such-and-such a physique, and their customs so-and-so. He had plainly connected in his mind as factors of health, good or bad, the *climate* of the place, the *race* of its inhabitants, their habits of eating, drinking, and clothing, their water supply, their housing. One thing is wanting: a statement as to the nature and number of the individual observations upon which the conclusions were based. As we shall see, *ad nauseam*, the one defect almost sterilized the many virtues.

In the *Books of Epidemics* we have again method and results, but here the method is more prominent than the results; on that account the *Books of Epidemics*, although not more remarkable products of pure intelligence, are of greater institutional value. These two books are short; the first, omitting an appendix of clinical records, occupies hardly twenty octavo pages, the third—again omitting the clinical records—not a dozen; they are descriptions of four *Constitutions* (the word has become classical, but perhaps owing to its modern implications we should do better to retain the Greek itself, *Katastasis*, which to us is colourless) in the island of Thasos. In each the method is the same. First a description of the weather (points of time are indicated by reference to the constellations visible so that they might be recognized by all Greeks, avoiding the confusion likely to be introduced by names of only local use), then of the prevalent illnesses and their clinical peculiarities. Sometimes there is no

difficulty at all in recognizing the illnesses. Thus in the spring of the first constitution: "Many had swellings beside one ear, or both ears, in most cases unattended with fever, so that confinement to bed was unnecessary. In some cases there was slight heat, but in all the swellings subsided without causing harm; in no case was there suppuration such as attends swellings of other origin. . . . The sufferers were youths, young men, and men in their prime, usually those who frequented the wrestling school and gymnasia. Few women were attacked. Many had dry coughs which brought up nothing when they coughed, but their voices were hoarse. Soon after, though in some cases after some time, painful inflammations occurred either in one testicle or in both, sometimes accompanied by fever, in other cases not. Usually they caused much suffering. In other respects the people had no ailments requiring medical assistance." That is a literal translation of Hippocrates' words; many readers know by personal experience precisely what epidemic illness he is describing, one which has certainly kept true to type for over two thousand years, and is neither more nor less serious in London in 1935 than it was in Thasos four hundred years before Christ. It is not, however, usually possible to live back into Hippocrates' world as in this instance; indeed, the ingenuity which has covered thousands of pages with "identifications" of the "diseases" observed by Hippocrates is, I think, misdirected. It would be as unwise for the epidemiologist to give time to it as for the serious student of history to devote much energy to guessing who wrote the letters of Junius. *Somebody* wrote those letters and they produced a great effect upon the British public, which is nearly all that matters. People in Thasos were ill, and ill in different ways at different times, which again is nearly all that matters. For what Hippocrates had in mind was to link up the variations of the illnesses with the variations of the *katastasis*, and by *katastasis* he plainly meant some general environmental conditions of which meteorological signs were indications. These two books are almost wholly objective—"The following were the circumstances attending the illnesses from which I framed my judgments, learning from the common nature of all and particular nature of the individual, from the illness, from the sick person, from the regimen, even from the prescriber; these make the diagnosis more or less favourable—

from the katastasis both as a whole and with respect to its parts of the weather and of each region," and so forth. These books are designed to furnish materials for such empirical correlation, showing that in such-or-such katastases such-and-such illnesses occur. The author is submitting to the scientific reader examples of a method of research by the prosecution of which materials for constructing a science of group aetiology, that is of epidemiology, might be ultimately garnered. There is no hint that he supposed the task to have been completed. The other four books of the Hippocratic collection which also bear the title Epidemics, no doubt contain notes and observations of the same author, perhaps copied from his private memoranda by a pupil—many, in the opinion of Galen, by his son; but even including these additional particulars we have still no more than examples of how to compile data. As we shall see later on, Hippocrates' method *was* exactly copied by epidemiologists two thousand years after his time, very closely copied by our own great physician Sydenham; yet in the opinion of many—an opinion I am philistine enough to share—knowledge of epidemiology was hardly further advanced when Sydenham died than in the age of Hippocrates. Let us try to discover why what was so nobly begun had so little success. I believe that a principal cause of failure was the lack of a statistical method. That remark coming from a professed statistician *ought* to recall the opinion of the cobbler on the virtues of leather; the onus of proof is certainly on me. Do I really think that if Hippocrates had supported his remarks on the prevalence of "swellings beside one ear, or both ears, in most cases unattended by fever" in the first constitution of Thasos by citing the numbers of patients he attended and the percentage so afflicted, his account of epidemic mumps would have been a scrap clearer? *Would* the lore of standard deviations, probable errors, and coefficients of correlation have helped him to realize more clearly the connection between katastases, temperaments, and ill health? I answer "No" to the first question and should but doubtfully answer "Yes" to the second question. But if one asked instead, Would the use of these methods by him have secured the continuance of his work by his successors? I can answer "Yes" without any hesitation at all. There are chairmen whose powers of grasping and interpreting sensory impressions are so excellent that a glance enables

them to declare, and declare rightly, that the ayes (or the noes) have it when the hands held up for either side seem to the ungifted equally numerous. But public opinion would be often misrepresented if all chairmen refrained from counting the hands. This would be so even if the chairmen were quite impartial; if they had previous convictions that the ayes were in the right the case would be worse. In the accumulation of particulars upon which to base an induction most of the collectors must be ordinary men, and a great many, all except the *very* stupid ones, must have conceived some hypothesis to describe or—as we loosely say—explain their facts. They are the commonplace, rather biased, chairmen sitting in the seat of the genius and it is long odds that if they copy him they will misrepresent nature's votes. They will be especially liable to do so if they suppose that they know what opinion the genius had formed of nature's ways. Such misfortunes did befall the successors of Hippocrates and were rendered more grievous by an event which I shall describe shortly. I do not think they would have happened if it had been possible—which it was not—for Hippocrates to employ the arithmetical method.

Although Hippocrates was an observer of nature and was described much later as the pioneer who separated philosophy from medicine, he was also a philosopher—I mean that one finds in his writings various speculative ideas. These ideas were not new in his day, some had become famous before his birth and they amounted to a working hypothesis. The hypothesis was that matter was composed of elements, the elements were earth, air, fire, and water; these elements had qualities the hot, the cold, the moist, the dry, and these qualities were predicated also of constituent “humours” of the body; these humours—blood, phlegm, black bile, and yellow bile—carrying the elementary qualities were, for this reason, attuned to the elementary qualities of the surrounding world, of the atmosphere, which again exhibited the states of being hot, cold, moist, or dry. All these notions are to be found in one or other of the Hippocratic books. In addition there is a doctrine, that of vital, animal, and vegetable spirits, essential to an understanding of ancient physiology but of less moment to epidemiology, so I will not now discuss it.

If we summarize what was known, what was proved, by Hippocrates, it amounted to this:

(1) It was definitely ascertained that epidemics of catarrhal disease and of pulmonary disease were commoner in the spring.

(2) It was proved that spells of warm, moist weather were in general very unhealthy, that in such weather pestilence was rife.

(3) It was known that at the autumnal equinox diseases again became prevalent. The first and third of these results of epidemiological observations can be confirmed in any year from observations made as far west as London; there is no doubt whatever about their truth, and I am afraid, so far at least as epidemics of catarrhal disease, common colds, and pneumonias are concerned, we hardly know any more than Hippocrates did about their general aetiology.

The second main observation, the unhealthiness of a hot, moist season, is also a truth which can be confirmed in the regions where it was made, that is in Greece or the Grecian archipelago, but it cannot be confirmed, because it is not a truth, so far north-west as England in our own time. The reason is that in the malarious countries warm, moist weather is extremely favourable to the breeding and dissemination of the insect porter of the basal illness and there is no doubt that an immense proportion of the illnesses reported by Hippocrates was malaria in one of its infinitely varied clinical forms. Indeed, although it is not true, as some have held, that the Greek word for fever always means malaria, it is probably true that more than three-quarters of Greek writings on fever are on malaria. Very unfortunately for epidemiology, the theory which Hippocrates used to explain the pestilential character of warm, moist weather was accepted and transferred to other countries.

Hippocrates died in or about 377 B.C., more than five hundred years before the next writer on epidemiology whose works have survived was born; in that long period there were many physicians whose names and some of whose discoveries we know. Most of them were certainly familiar with the Hippocratic books, and it is strange if some did not consider whether what was begun in the Books of Epidemics might not be continued. There flourished a whole school of physicians whose principles would

seem to compel them to adopt Hippocrates' epidemiological method. These were the Empirics, whose rule, the "Tripod of the Empirics," was to depend upon:

- (1) One's own observations.
- (2) The observations of others, contemporaries or predecessors.
- (3) Analogy.

The empirics were very contemptuous of pure theory; one does not become either a farmer or a navigator, they said, according to Celsus, by arguing the point, nor can one become a doctor that way. The empirics of whom we know anything—and that is very little—were what the British public call doctors; they were practising physicians and surgeons—some of the best clinicians of their time apparently—and if they did ever apply the tripod to epidemiology, either they carried knowledge no further than Hippocrates left it or—which is perhaps equally likely—what they discovered seemed neither interesting nor important to their contemporaries and was forgotten. We do not *know* that anything more was done with epidemiology until over five hundred years after the Books of Epidemics were published, until the lifetime of Galen of Pergamos, who was born in A.D. 131 and died in the reign of Septimius Severus, probably between 201 and 210.

Distance in time as in space foreshortens objects; it would not seem odd if anyone now spoke of Chaucer or Langland as an ancient writer, but it does give one a shock to find Galen speaking of Hippocrates as an ancient writer. Galen lived so long ago that we tend to picture him as a sort of younger brother of Hippocrates, although Hippocrates was as far from him as Chaucer is from us. In that time much had happened and the happenings had not been favourable to the development of scientific epidemiology. Tares had been sown with the wheat in ancient Hellas; they had not indeed choked the noblest harvest which men have ever garnered, all of it has not yet been garnered, but they had fouled the soil which had become very dirty by the second century of our era. A particularly rank weed, especially dangerous because in trying to rid the ground of it we may uproot valuable plants, was intellectual self-sufficiency, the notion that by sheer force of

reasoning one can grasp truth without laboriously searching for it. The very great Greeks, even Plato, even Hippocrates, were not free from that infirmity; the Greeks of the first centuries A.D., according to Paul of Tarsus and to other less distinguished observers, were far gone in the complaint. *Corruptio optimi pessima* is a horrible truth. Juvenal's scorn of the hungry Greeklings may be exaggerated, but patient modern scholars, such as Haeser and Sir Clifford Allbutt, have not found much to be said in favour of the doctors at Rome (nearly all Greeks or Greek-trained), whether morally or intellectually. It is not an inspiring time when it is high praise to be able to say of a man that he is not *known* to have poisoned anybody. Cicero admired Greek literature even more than he admired himself, but expected nothing of Greeks; his character of the Greeks (in his correspondence) does not reveal deep moral obliquities but a mental sharpness—very different from sagacity—a lack of intellectual honesty and straightforwardness which we may accept as typical of the clever alien parasite upon an unimaginative plutocracy, that is, typical of the Greeks in Roman civilization; Galen was to some extent true to type. We know much more of him than of many physicians of our own century—far more than we know of Sydenham—he has revealed himself almost as fully as any man, and it would be easy to quote pages of smart ungenerous witticism and dialectic, mere cleverness without sagacity.

Galen's highest title to a place beside the great masters is that in spite of his age and his own temperament he did much work not unworthy of Aristotle or Vesalius. He was a great experimental physiologist and practical comparative anatomist; as great as, perhaps greater than, any Greek of either the classical or Alexandrian period. Verbalism and dialectic there was in his physiology, false analogy in his anatomy, but there was real scientific experimentation in the one and laborious, accurate dissection in the other. But we are concerned only with his epidemiology, and of this we can say that the harm he did has not yet been undone. Galen had to choose between theory and practice. He might have applied the Hippocratic *method*. He lived in a great city state and actually experienced one of the great outbreaks of bubonic plague known to recorded history. The epidemic history of Imperial Rome could have been

under his hand a very splendid continuation of the epidemiological annals of Thasos, the fruit of laborious but well-spent years. That task he declined; hardly any epidemiological *observations* of any kind and no systematic epidemiological observations are to be found in all his books. There was a very different thing he could do. The Hippocratic books contain some theorizing about epidemics, and this theorizing might—without any but mental labour—be welded into a system. This task he performed, and so efficiently, that the fetters he contrived have only just ceased to bind us—if, indeed, they have so ceased. Galen's system (every element of it is derived from some predecessor, only the systematization was his own) was this: Ill health depends upon the interactions of three sets of factors. The first, and most important, set is given by the innate qualities of the body, its *crasis* or, in the Latin word which has become familiar, *temperament*; the second a medley of factors, such as vices of eating or drinking, habits of life, etc., the *procatarctic* factors; the third, states, *katastases*, or, as we badly say, *constitutions* of the atmosphere. The temperaments depend upon the blending of four elementary qualities, the hot and its opposite the cold, the moist and its opposite the dry. Harmoniously blended we have the perfect temperament or *eucrasis*, and there are eight discords, four when one quality only is in excess, four more when two are in excess. The *procatarctic* factors are manifold, but the *constitutions* are also referable to four qualities and so may give eight discordant and one harmonious result. I think a reader will say of this bald description that it sounds like a rather silly Christmas game, and indeed acuteness without wisdom *is* the silliest thing in the world. But use the counters of your silly game with skill and something may be made of it. Very few of us can remember learning the moves of chess; if we learned them for the first time as grown men we should—quite rightly—deem them absolutely arbitrary and perhaps also—but quite wrongly—think that they could not lead to a game so interesting that clever men sometimes give their lives to the playing of it. Galen developed a very clever game and he made it seem real. Just as some chess writers have pretended that by playing chess one may become a military strategist (Napoleon played chess so badly that his suite sometimes found it very hard to lose to him), so Galen pretended—perhaps believed—that his

counters, hot and cold, moist and dry, were real money—that is where blood, phlegm, black bile, and yellow bile come in—and this is how he did it:

“For the rest, the warmer *katastases* of the atmosphere around us, such as are most likely to occur about the rising of Sirius, when inspired evidently inflame the heart; impinging upon the body from without they warm it as a whole, in particular the arteries which absorb not a little of the aerial substance; from all of which the heart must be at once affected and be immoderately heated, acquiring a maximal degree of febrile affection, and impregnate therewith the whole body. Indeed, given a pestilential *katastasis*, inspiration is the principal factor. For sometimes the fever is generated through the humours which are ripe for putrefaction when the animal has experienced the exciting cause from the atmosphere, but mostly the origin is inspiration of air infected with a putrid exhalation.

“The beginning of the putrescence may be a multitude of unburned corpses, as may happen in war; or the exhalations of marches or ponds in the summer; sometimes it is the immoderate heat of the air itself as in that pestilence of which Thucydides writes: ‘A corruption seized the bodies of men in their close and ill-ventilated hovels. The starting-point of the pestilence was the preparation for putrefaction of the humours of the body due to bad food. It may be, too, that atmospheric continuity was a factor, that products of putrefaction came from Aethiopia which were destined to be a cause of fever in the persons whose bodies were prepared to sustain this injury.’ Always this is to be remembered, that no cause can be efficient without an aptitude of the body; otherwise all who are exposed to the summer sun, move about more than they should, drink wine, get angry, grieve, would fall into a fever. Or, again, all would fall sick at the rising of the dog star, and in a pestilence all would die. But, as I have said, the chief factor in the production of disease is the preparation of the body which will suffer it. Let us imagine, for instance, that the atmosphere is carrying divers seeds of pestilence, and that, of the bodies exposed to it, some are choked with excrementitious matters apt in themselves to putrefy, that others are void of excrement and pure. Let us further suppose an obstruction of orifices and resultant plethora in the former, likewise a life of luxury, much junketting, drinking, sexual excess and the crudities which must attend on such habits; in the latter let us suppose cleanliness, freedom from excrementitious matters, orifices unobstructed and uncompressed, desirable conditions, as we may say, free transpiration, moderate exercise, temperance in diet. All this being supposed, judge thou, which class of body is the likelier to be injured by the inspiration of putrid air. Is it not plain that the former class from the first inspiration will receive a beginning of putrefaction and that bad will go to worse, while those which are pure and void of excrement will either escape altogether or

suffer so little damage as easily to return into the way of nature? Hence then, although, so often as the *katastasis* of the atmosphere departs from its proper nature into the hot and humid, pestilential diseases must needs arise, yet will those chiefly be affected who were beforehand saturated with excrementitious moisture while those who labour moderately and are temperate in diet remain refractory to such diseases. This has been said of one example, but it is an universal truth.”\*

I think it will be seen that the game is not so silly as its rules might lead one to suppose. Indeed, it is very much like chess. There are qualities possessed by a consummate chess player and exemplified in his play which are very valuable to a commander-in-chief; there are things in that passage I have quoted—e.g. “no cause can become efficient without an aptitude of the body”—which the epidemiologist as well as the doctor should burn into his mind, but men never put chess players in command of armies merely because they were chess players, they did not think chess *was* war; they did think Galenical epidemiology was really epidemiology. Indeed, I am not quite sure that my friend Sir William Hamer might not say that I and my statistical associates only wish to substitute for Galen’s game another game with even more complicated rules, so that in criticizing Galen I am perhaps really pickling a rod for my own back. It is only a game, not because Galen never mentions facts of observation, what actually happened to sick people—he mentions then often enough—but because he fits them into his system instead of founding a system on his observations. I pointed out that, starting with the Hippocratic books, a great patient-minded man, someone like Francis Galton, might have developed a system of descriptive or even quantitative epidemiology. But it would have been a still more extraordinary man, even more original minded than Galton, who, after soaking his mind with Galen’s commentaries upon Hippocrates, still thought there was anything left to do. The problems were *all* solved. Many people who went over the ground in the next fifteen hundred years were very able men—only the ignorant suppose that all mediaeval writers were credulous fools—it occurred to none of them that there *were* any unsolved problems of epidemiology. True they could not

\* *De Febrium Differentiis*, Kuehn’s Edition of the works of Galen, Vol. VII, pp. 273 et seq.

prevent people catching plague, but they had a perfectly satisfactory theory of plague, and, after all, even we cannot always prevent epidemics of plague either.

They felt that their practice was unsuccessful, but their faith in the intellectual theory was never shaken. When the scientific hegemony passed from Greek to Semitic civilization, new material for epidemiological thought was collected. The facts collected by Arabic-speaking physicians—by Rhazes and by Avicenna, among others—are more valuable than any even in the Hippocratic *corpus*—nobody until Sydenham gave a better natural history of smallpox than Rhazes—but the epidemiological theories of the Arabians and Arabists were merely bad copies of Galen. It is significant that the one branch of science which advanced, was improved, was mathematics. In that field the tares did not choke the wheat, there were never any dark ages—by which I mean ages when the best living exponents were *certainly* inferior to the average of some previous age. But although Galen himself was an enthusiastic mathematician he did not apply quantitative methods to epidemiology, and epidemiology had no share in mathematical development.

The story of epidemiology from the third to the sixteenth century is the story of one man's thoughts, originally not first rate, and finally, by repetition, gloss, translation, re-translation, become a mere jargon. So that the first real advance was a conscious step backwards, the step taken to discover what Galen's opinions really were.

#### RECOMMENDATIONS FOR FURTHER STUDY

The works of Hippocrates are included in the Loeb Series, and those who (more fortunate than I) are sufficiently good Greek scholars *really* to care about textual accuracy should read Hippocrates in this edition. For literary enjoyment, however, Littré's version is not likely to be superseded, while Francis Adams' translation in the old Sydenham Society's series is excellent.

There is no modern edition or translation (into English) of the writings of Galen which are of epidemiological interest. The unscholarly reader will find some first aid in my own (unscholarly) paper in the *Proceedings of the Royal Society of Medicine*, 1921, Vol. XIV (Section of the History of Medicine, pp. 3-16). Clifford Allbutt's *Greek Medicine at Rome* should be read. Those (still, I am

optimistic enough to believe, a large number) who can read Latin comfortably will find that some of the translations of Galen's best writings are good, some barbarous. They are to be found in any large library, and the student need not be daunted by folios; one soon grows accustomed to abbreviations. The same class of reader should not miss the introductory chapter of Celsus' *de Medicina*, the best written short history of medicine before Galen.

## II

### FROM THE REVIVAL OF LEARNING TO GRAUNT

THOMAS LINACRE, the first president of the London College of Physicians, took a step towards freeing us from Galenism. The garden of Looking-Glass House is not the only place where in order to meet the person you wish to meet it is best to walk the other way. Linacre, who believed an ideal Galen to have the key to all medicine, walked straight up to the real Galen; probably before Linacre not a dozen west European physicians since the fall of the Roman Empire had read a dozen pages of any book by Galen in the original language. Linacre translated several of Galen's most important works into a Latin which, Erasmus said, was better than the Greek, and has at least not been improved upon since (only *one* of Galen's treatises has ever been translated into English). This made it possible for all physicians to read Galen for themselves, and it is probable that most modern physicians—for instance Sydenham—studied Galen in that way. The same service was rendered to Hippocrates, and once more a choice was offered to the medical world—Will you follow the *method* of the constitutions of Thasos or will you believe the gloss of the Pergamite?

For some time it looked as if the old choice would be retained. Scholarship revived before science. The contribution of Linacre, the first president of the new college, was purely literary; his successors during the next fifty years are now only names. The next great president and the first to contribute to the literature of epidemiology was John Kaye of Norwich, best known as Dr. Caius, nine times president, who died in 1573. Caius' treatise on the English Sweat, first printed in English in 1552, and subsequently, in a revised form, in Latin, is the first original work on an epidemiological theme of an English physician; it enjoyed a great reputation and was reprinted as recently as 1721. Hecker spoke of it favourably, but no reader of our age could do so. Its quality may be illustrated easily enough. The English Sweats were, in the opinion of Sir William Hamer and the late Dr. F. G. Crookshank, influenzas. Clinically they were characterized by

an intense fever ending rapidly in death or convalescence. Caius set out a number of points to be investigated, among others why the disease was of short duration (*morbis diarius*). His explanation is as follows.\* There are two genera of *vis venenata* originating in putrefaction and of a contagious character, the one of a subtler and acuter, the other of a denser and milder kind, the difference depending on the nature of the substance which putrefied. What happened was that the humid part of the substance undergoing putrefaction was attenuated by external heat and converted into a spiritus; according to the nature of the fundamental substance, whether loose or compact, so would be the nature of the *vis contagiosa*. Now, for the reception of this force one had in the body two seats, the animal spirits and the humours. By spirits, Caius would have us understand certain subtle, aerial, moist, and warm vapours of the blood; by humours—just the humours. Clearly then the first sort of *vis* has by analogy an affinity with the bodily spirits as defined, the second sort with the humours. Hence the second sort of *vis* will generate plague (clinically both what *we* call plague and what *we* call typhus); the first sort, if other conditions are favourable, an ephamera, or short fever. The humours Caius compares to moist wood, slowly ignited, and, when ignited, burning slowly; the spirits he compares to flax, which burns quickly. We can now understand the suddenness of the contagion in the Sweat: it is due to inspiration and expiration of vitiated air. That also explains why many fall sick together, why symptoms succeed one another rapidly, why there is no abscess formation, and why death (or recovery) follows within a few hours. Caius was a good scholar; he had read Galen in the original text, yet his epidemiology is just as much a mere verbal jargon as that of his mediaeval predecessors who knew no Greek. Compare this jargon with the language of an original-minded man whose book was published nine years before that of Caius. Fracastori's positive scientific knowledge was no greater than that of Caius; factually he was no better equipped, but he had scientific intuition. He could not rest satisfied with verbalisms anent heat and putrefaction. "If," he asks, "a house on fire sets its neighbour alight, should we speak of that as contagion?" and

\* See pp. 36 et seq. of Joh. Caii, Britannii, *de Ephamera Britannica*, edition of 1721.

replies that we should certainly not do so because here it is the destruction of a whole by a whole, and besides we conceive a contagion as something following an infection, which latter takes its origin in certain minute invisible particles. Fracastori accordingly reaches this account of contagion in general. "Contagion is, then, a passive phenomenon undergone by a compound substance. But compounds may be destroyed in two ways; in the first place by the advent of something incompatible with the stability of the compound, in the second place by the actual dissolution of the compound, as happens in putrefactions; so there is no need to inquire by which means contagion occurs, infection having been brought in by the minute particles; further, we are to ask: What is the nature of infection? Are the particles corrupted or merely altered? What, in a word, happens to them? Hence we are led to inquire whether every contagion may not be a species of putrefaction. All these matters will become clearer when we have examined the characteristics and causes of various contagions. If we are allowed to offer a provisional definition of contagion, we should say that contagion was a corruption of the substance of a compound passing from one to another in precisely the same form, derived from an infection generated originally in insensible particles."\*

This breathes a spirit very different from Caius' Galenical distillation. But Fracastori was more than two hundred years before his time; indeed, even at the beginning of the nineteenth century his book would not have found a dozen sympathetic readers. An event needs the man *and* the hour before it can happen. "It takes two to speak truth—one to speak and another to hear."

But while Caius was president of the London College another physician was making notes of his cases in Paris; those notes were printed many years after his death by his nephew Thevart. The two books of Epidemics of Guillaume de Baillou, sometime dean of the Paris faculty, printed in 1640, are the first contribution to epidemiology on the Hippocratic model which is certainly worth reading. I am not sure that it has directly influenced English epidemiological literature; Sydenham never mentions

\* See *Les Trois Livres de Jerome Fracastor sur la Contagion, etc.*, edited and translated by L. Meunier, Paris, 1893, pp. 5-7.

de Baillou—or Ballonius—although Sydenham's plan is very like that of Ballonius—this, however, may easily be due to both having followed the Hippocratic model. Ballonius meant his book to be published, for he left a preface which seems to me a much finer piece of writing than the deliberately fine writing of John Caius or of the pompous latinist who gave Sydenham's notes the form in which we have them. Ballonius said we ought not to act like the beasts that perish, but should make notes of what we see so that we shall not be always taking forms of illness for something new and be startled by new bogies (*ut cum morgi hujus aut illius indolis inciderint, aliquid novum contigisse non dicant et novorum morborum, tanquam incogniti cujusdam monstri accessu ac fronte non terreantur*), and, as his contribution, he transcribed his day book of medical experience during ten years in Paris, beginning in 1570 and ending in 1579. At last, after more than two thousand years, one has a man writing down what he saw, what he thought, and what puzzled him. Most readers will, I think, be fascinated by the writer's personality, and will also understand why he failed, and perhaps why without statistics his task cannot be executed. He sets himself to do what Hippocrates tried to do. He will record the weather of the seasons, the kinds of illness he observes, and how one type of prevalent sickness changes into another. *But* he is a human being like ourselves, he is treating sick fellow-creatures—some die, some recover; he is not a machine or a god, he cannot preserve an Olympian impartiality, he must ask himself what is the right treatment in the particular case. What ought one to have done for Lady Du Plessis who had pains for twenty months? John Bellicant again, *he* had pains, and when we opened his body the muscles of his arms were smothered in fat—"a thing I have noticed in others with similar pains, which no art would relieve, what is one to do? What is the cure?" The reader—like the writer—is soon much more interested in the personal stories of these Parisians of three hundred and fifty years ago than in the epidemic constitutions. It seems that we must drape our cases in an arithmetical cloak, turn them into numbers and percentages or their mere humanity will be too much for us. If one tries to do this by making a synopsis, the essence evaporates. I have tried it, and am reduced to finding that, for instance, there was a wet

spring in Paris in 1571, and many people had colds and many pleurisy, and there were sore throats and inflamed tonsils and bleeding didn't help in pleurisy. That great historian of medicine, Heinrich Haeser, writing of Ballonius (II, 139), says that his Epidemics "were a worthy prelude to the work of the English physician, Thomas Sydenham, which appeared a hundred years later, far behind whom, indeed, Baillou, with his slavish subservience to the authority of his Greek model, halts." In my opinion this censure is unjust to the French physician, but there is no doubt that Sydenham has had immensely more influence upon the development of epidemiological ideas than Ballonius, so much more that I may pass at once from Ballonius to Sydenham, and ignore the intervening observers such as Peter Foreest.

Sydenham began a new epoch in the history of medicine; there is something of Looking-Glass House about medicine. To encourage the cult of Galen it was rash to secure the wide circulation of his works, but it took more than a century to prove how rash it was. Men before Sydenham, for instance Paracelsus, had rejected Galenism. Jerome Fracastori, as we have seen, published in 1546 the most original contribution to epidemiological knowledge which appeared before the eighteenth century, but Sydenham was the first academic physician of high repute to assail Galenism directly. Even Sydenham, indeed, was not a root-and-branch man; in fact, in pathology he was not in front of but behind his age, he regarded experimental physiology with contempt, the doctrine of humours is implicitly accepted by him, and the notion of temperaments. But he was firmly convinced that "this art [of medicine] was in no way better learned than from its practice and its exercise; and that, in all probability, he who devotes his eyes and mind to the natural phenomena of diseases will succeed best in eliciting true and authentic indications of treatment" (dedication to Mapletoft, written in 1675). Having this faith, he had no use at all for glosses and comments; one must learn from the observation of patients, not from books. So Sydenham, like Hippocrates on Thasos and Baillou in Paris, decided to record his observations, and has left a book which has had, directly and indirectly, an enormous influence upon the minds of physicians and epidemiologists.

Since, for reasons which I shall shortly give, I think the value

of Sydenham's epidemiological work has been overrated, I wish to make it clear that Sydenham's primary interest was clinical; he was a practising physician, not an arm-chair philosopher or even a medical officer of health. He was concerned to treat patients; he believed (a revolutionary belief) that he could not treat them properly unless he learned by observation how illness developed naturally, unless he adopted the Hippocratic method. If every word he has written about epidemic constitutions were omitted from his writings, his works would still be among the classics of medicine. His account of smallpox and his principles of treating it are, by the consent of all the great physicians since his time, masterly.

But we are only concerned with his epidemiology. Sydenham's epidemiological teaching was this. Owing to mysterious and, he thought, inexplicable changes in the atmosphere we have constitutions, *epidemic constitutions*, characterized by *stationary fevers*; these stationary fevers may graft themselves upon any illness which, being independent of the epidemic constitution, he called *intercurrents*, or may exist alone; they set their characteristic seal upon all illnesses prevalent during the reign of the particular epidemic constitution. Hence, he supposed that illnesses in different years which are called by the same names will run utterly different courses and require utterly different treatments. "I must observe," he says, "that when any constitution generates various species of epidemics these are essentially different from those bearing the same name but produced by another constitution."\* We may put it, very shortly, thus: diseases which, judged by ordinary rules of diagnosis, are the same in different years, say a case of "pleurisy" or even a case of "smallpox," may (if the two years are under the influence of different constitutions) be so essentially different that treatment which is successful in one will completely fail in the other. "Nothing," says Sydenham, "I suppose has more astonished the student of medicine than the protean character of epidemic diseases, not so much as referable to differences of weather as to differences of epidemic constitution in different years upon which they depend. This very evident diversity of the diseases in question is seen in respect both of symptomatology and of necessary treatment. From which it

\* *Obs. Med.*, 1, 2, (18).

plainly appears that diseases which to the inattentive observer may seem congruent in respect of both external features and symptoms will be found by a judicious scrutiny to differ as chalk from cheese. I do not, indeed, know whether a sedulous examination (for properly carrying out this the brief space of man's life were hardly sufficient) might not teach us that certain epidemics succeed one another in a series, forming as it were a circle, or alternatively that, owing to an occult diathesis of the atmosphere and a mysterious succession, they attack us indiscriminately. This only, fortified by a multitude of exact observations, I do confidently hold, that the aforesaid species of disease, in particular the continued fevers, may vary so enormously that you may kill your patient at the end of the year by methods which cured sufferers at the beginning of it."\* Such, very briefly, was Sydenham's contribution to epidemiology. We have first to consider what essential value it possesses, and next how it actually influenced medical thought. On the first point, it is clear that Sydenham contributed nothing to knowledge of the *aetiology* of epidemic disease; his atmospheric constitution is no more intelligible than the constitutions of the Greeks, perhaps it is less intelligible, for it is at least doubtful whether Hippocrates meant by atmospheric constitution more than what we should call meteorological conditions.

Again his quite positive statements respecting the clinical convergence of "different" diseases to a common type under the influence of a reigning constitution, in particular his assertion that the "same" disease needed quite different treatment when the epidemic constitution altered, are certainly not unchallenged. An able younger contemporary, Freind, pointed out that although Sydenham *said* all this his recorded clinical practice, particularly with regard to the continued fevers, did not seem to vary. While such observers as Goodall in our own time, with special opportunities of studying the clinical types of reigning illnesses have not perceived a clinical convergence. "Providence," writes Dr. Goodall, "has granted me a clinical experience of forty years of epidemic diseases, the diseases in which the phenomenon should especially be manifest, and experience which has been gained almost entirely in one place, that is, London, so that my obser-

of Sydenham's epidemiological work has been overrated, I wish to make it clear that Sydenham's primary interest was clinical; he was a practising physician, not an arm-chair philosopher or even a medical officer of health. He was concerned to treat patients; he believed (a revolutionary belief) that he could not treat them properly unless he learned by observation how illness developed naturally, unless he adopted the Hippocratic method. If every word he has written about epidemic constitutions were omitted from his writings, his works would still be among the classics of medicine. His account of smallpox and his principles of treating it are, by the consent of all the great physicians since his time, masterly.

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plainly appears that diseases which to the inattentive observer may seem congruent in respect of both external features and symptoms will be found by a judicious scrutiny to differ as chalk from cheese. I do not, indeed, know whether a sedulous examination (for properly carrying out this the brief space of man's life were hardly sufficient) might not teach us that certain epidemics succeed one another in a series, forming as it were a circle, or alternatively that, owing to an occult diathesis of the atmosphere and a mysterious succession, they attack us indiscriminately. This only, fortified by a multitude of exact observations, I do confidently hold, that the aforesaid species of disease, in particular the continued fevers, may vary so enormously that you may kill your patient at the end of the year by methods which cured sufferers at the beginning of it."\* Such, very briefly, was Sydenham's contribution to epidemiology. We have first to consider what essential value it possesses, and next how it actually influenced medical thought. On the first point, it is clear that Sydenham contributed nothing to knowledge of the *aetiology* of epidemic disease; his atmospheric constitution is no more intelligible than the constitutions of the Greeks, perhaps it is less intelligible, for it is at least doubtful whether Hippocrates meant by atmospheric constitution more than what we should call meteorological conditions.

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\* *Obs. Med.*, I, 2, (1-3).

vations have not been subject to the disturbing influence of changes of locality. Further, two years or so ago, when I was refreshing my memory of the doctrine I am now discussing, I paid especial attention to the cases admitted to the North-Western Hospital at Hampstead during the winter and spring of 1924-5. Influenza was the stationary fever of the period; whooping-cough, scarlet fever, diphtheria, mumps, rubella, and chicken-pox were the intercurrents amongst the infectious diseases. I found no evidence whatsoever that these last-mentioned diseases bore any trace of influenza, and that experience was the experience of former years.”\* On the other hand, another experienced contemporary, Sir William Hamer, has expressed as high an opinion of Sydenham as an epidemiologist as Boerhaave had of Sydenham the physician.

It is not really hard to explain these conflicts. We judge, and must judge, the value of any man's work in accordance with our psychological make-up. We really ask ourselves whether this way of looking at things enables us to overcome difficulties of which we are conscious. To those who feel that exact description, close contact with the data of immediate observation, and analogical reasoning from experimental data are the fundamentals of science, Sydenham's *Weltanschauung* becomes the more repugnant the more closely it is examined. They perceive that his reasoning is loose, his observations—however accurately they may have been *made*—not precisely recorded, and that he despised and ignored the experimental and statistical methods of research which some of his contemporaries had already begun to fashion. But there are others, not less intellectually gifted, not less loyal servants of science, who perceive how short-sighted and pragmatic is a good deal of “exact” and experimental science. They recognize that very bad reasoning may be hidden behind very good algebra, and that the oddest things are done in the name of the crucial experiment. They see that Sydenham did conceive of epidemics *sub specie aeternitatis*, had something of the fine audacity of the Greeks, did believe that there was an *order* in epidemiological phenomena. To them the concept of a secular change of type, that there is a continuous change in the whole complex of events the *differentiae* of which can be assigned, is

\* *Proc. Roy. Soc. Med., Sect. Epidem., Vol. XXI, 1927, p. 125.*

something more than rhetoric. They think they can show that before the emergence of each pandemic of influenza there have been signs and wonders:

*"Tempore quamquam illo tellus quoque et aequora ponti,  
Obscenaque canes, importunaque volucres  
Signa dabant"*—

which may be interpreted by those who are not too busily engaged in "stamping out" epidemics or crucially experimenting in laboratories, and too confident that scientific observation is less than a century old to pay attention to history.

It is that aspect of Sydenham's work which appeals to a few men in every generation, and only those of us who think that *A Grammarian's Funeral* is silly will sneer at it. But it is not to sneer at the Grammarian to affirm that it is better for the low man to seek a little thing to do and do it, to go on adding one to one and actually reach a hundred, than to resemble the high man only in failure. The high men are rare, the low men common; if we ask what the doctrine of epidemic constitutions has taught us, the low men, I think it has taught us very little. Some of us, perhaps, it has taught one good lesson, to be humble-minded, to admit that there may be a generalization we cannot grasp. But knowledge of the less remote aetiological factors of epidemic disease, of the role of infected water in typhoid, of insect porters in plague and malaria, of most that has been of direct service to man in prophylaxis, has been discovered by methods which, in their infancy, Sydenham disdained. Perhaps we might apply the remark of Macaulay. "Plato drew a good bow, but, like Acestes in *Virgil*, he aimed at the stars, and therefore, though there was no want of strength or skill, the shot was thrown away. . . . Bacon fixed his eye on a mark which was placed on the earth and within bowshot, and hit it in the white." For Plato we may substitute Sydenham and for Bacon—whom? I suggest an obscure London tradesman named John Graunt, who died in distressed circumstances some years before Sydenham. The reader may, perhaps, have wondered whether a physician recording the epidemic constitutions of London in the seventeenth century had any advantages over his model of Thasos two thousand years before with regard to the possibility of telling *how many* people

died when the constitution was pestilential. That there were some means one would gather from Sydenham himself, because he says twice that in one week of the Great Plague year some eight thousand died; but with this exception one does not find arithmetical statements. It is time to consider what were the data of a statistical kind which Sydenham could have used.

By the end of the seventeenth century it was possible to form a fair estimate of the number of people who were born or had died in most parts of the country. Henry VIII's Minister, Cromwell, issued an order that all parish clergy should maintain a register of those they christened, married, or buried, and this order was repeated by Queen Elizabeth. In many parishes, of course, the order was disobeyed, but in a large number it was actually carried out, and parish registers going back to the middle of the sixteenth century are fairly common. In the middle of the eighteenth century Dr. Thomas Short collated many of these and drew some interesting conclusions from them. In days when internal migration (except to London) was slight, and people were, or said they were, of one mind in religion, a parish church register was not a very bad substitute for a statistical office. Of course, even then it recorded both births and deaths incompletely. Children who died unbaptized usually escaped the statistician, except a proportion entered as chrisoms; persons buried in unconsecrated ground, for instance in the burying grounds of dissenters, escaped altogether. However, a good deal of information about the movement of local population might have been gathered from a study of parish registers if anybody had thought it worth while to look for it. But down to Graunt's time nobody did think so.

In London much more elaborate data were systematically compiled: the famous Bills of Mortality. The first of this series was prepared in 1532, and tells how many "syns the 17th day of November unto the 23rd day of the same month is dead within the city and freedom yong and old these many folowyng of the plague and other diseases." It accounts for less than seventy deaths and is not at all likely to be complete, but it is the first of a very interesting series. In the next thirty years Bills of Mortality were issued irregularly and probably only when plague was epidemic, but after 1563 they were probably regularly kept, and after 1592 this was certainly the case. In 1625 the Company

of Parish Clerks obtained a decree of Star Chamber to set up a special printing press for the issue of both weekly and annual Bills of Mortality. At first deaths from plague and all other causes were noted, without distinction of sex, and the number of christenings. In 1629 causes of mortality other than plague were particularized and the sexes were distinguished (not under causes, but for total deaths). In 1727 the ages of the deceased were first recorded, and no other change occurred until the Bills ceased to be issued, which was in 1849, by which time they had long been superseded by the publications of the General Register Office.

When the first Bill was made one hundred London parishes were included—a number which had increased to one hundred and eight by 1563 and reached one hundred and twenty (ninety-six within the City walls) by 1604—sixteen parishes were without the walls, but within the ancient liberties, and a further group of nine out-parishes in Middlesex and Surrey were reported on. In the year 1626 the City of Westminster was brought in, and in 1636 Islington, Hackney, Stepney, Rotherhithe, Newington, and Lambeth were included. In Graunt's day the total of parishes was one hundred and thirty, which covered the whole population of London and the immediate suburbs in the seventeenth century.

These documents, which were as familiar to educated Londoners as *The Times Literary Supplement* is to us, were of course in the hands of Sydenham, but with the exception mentioned I do not recollect any reference to and certainly no quotation from them in his chronicles. As a professional man he no doubt despised the diagnoses from which the statistics of deaths by causes were compiled. These diagnoses were made by old women, some of whom were drunken, others venal, and all ignorant. Still, even an ignorant and drunken old woman is likely to be right on the fact of death in most cases, so that the weekly totals of deaths would, it might be supposed, have some value. But Sydenham does not seem to have thought so and in this respect was not an exception. Hardly anybody else thought so either. I think I have read somewhere that there was a little betting on the weekly figures—horse-racing was in its infancy and one must bet on something—but no other use seems to have been made of the statistics.

But in the year 1662 a little volume was published. Its author

was very apologetic, but pleaded in extenuation that "there is much pleasure in deducing so many abstruse and unexpected inferences out of these poor despised Bills of Mortality, and in building upon that ground, which hath lain waste these eighty years. And there is pleasure in doing something new, though never so little, without pestering the world with voluminous transcriptions." This modest author was John Graunt.

#### RECOMMENDATIONS FOR FURTHER STUDY

The bad and the good sides of epidemiology in the age still dominated by the ideas of the scholarly humanists will be conveyed by a comparison of Johannis Caii, Britanni, *de Ephemera Britannica*, Lib. I (essentially worthless), and Ballonii, *Epidemiorum et ephemeridum*, Lib. II (more objective, in my opinion, than Sydenham's epidemiology and very different from Caius).

Sydenham himself is an accessible writer. Greenhill's edition of the *Opera Omnia* is far the best; the English translation made from this text by Latham deserves Dr. John Brown's (the Dr. Brown, author of *Horae subsecivae* and some excellent essays on Sydenham and Lockef unfavourable criticism. Dr. John Comrie's *Selected Works of Thomas Sydenham, M.D.*, London, 1922 (Bale, Sons and Danielsson), is much better. Payne's biography of Thomas Sydenham (London, 1900) is the work of a good scholar.

The case for regarding Sydenham as a far greater epidemiologist than I think he was will be found in Sir William Hamer's *Epidemiology Old and New* (London, 1928), which, with the other papers by its author and by Dr. F. G. Crookshank cited in it, should be carefully studied.

For the whole period covered in this chapter Haeser's *Lehrbuch der Geschichte der Medicin* (Jena, 1881) is invaluable.

### III

#### GRAUNT AND AFTERWARDS

JOHN GRAUNT, the son of a London draper and himself for many years a prosperous City shopkeeper, is one of the great men of science. Partly because he was not, in the bookish sense, a learned man, partly because before he died he fell on evil days and became poor, partly because a friend and protégé of his, William Petty, achieved a reputation as a statistician and—what was more to the purpose—made a fortune and founded a family, Graunt's reputation was overshadowed. Soon after his death a suggestion was made that Graunt's works were really written by his friend Petty, and this quaint paradox has been gravely maintained down to modern times. Any statistician acquainted with the publications of the two men would be as easily convinced that Petty wrote Graunt's masterpiece as a mathematician could be convinced that Einstein's papers were really composed by Herr Emil Ludwig. Graunt's contemporaries might have been pardoned for failing to recognize his ability, but to do them justice they did not fail.

Graunt *was* recognized. His work was approved by the Royal Society and he was elected a Fellow. In mere numbers competition was not so keen in the seventeenth as in the twentieth century for the honour of writing F.R.S. after one's name. But the Royal Society enjoyed very distinguished patronage, its most influential members attached more importance to social distinctions than they do now, and the old story of King Charles' comment at least proves that Graunt's selection was a rare honour. Graunt, as I have said, had to work upon data of, in the medical sense, poor quality, so that his positive contributions to knowledge were mainly concerned with the influence of *age*, *sex*, and *locality* upon what we should call now the rate of mortality from all causes. He first demonstrated vital statistical facts which now seem to us commonplaces, such as the high rate of mortality in infancy, the usually higher rate of mortality in the country than in the towns, the excess of male births and the subsequent equalization in numbers of the sexes, mainly through the higher *post-natal* rate of mortality upon males. This last discovery had a great

influence upon the subsequent development of vital statistics. Its justification of the ways of God to man appealed to two theologians, one of whom, the Prussian chaplain Johann Peter Süssmilch, sowed Graunt's seed in Germany and reaped a harvest. Another of Graunt's discoveries, this time of a *method*, had a still greater effect. Although the notion of what the Germans call an order-of-dying-out, the idea of following out interval by interval a number of persons born at the same instant and of noting how long it is before all of a generation are dead, is simple, and it is possible that some practical rules found in the writings of Roman jurists were based upon observations of actual sequences, Graunt was the first person who employed the statistical method. The difficulty is to see how from the records of general mortality one can deduce anything analogous to the case of the dying-out of a generation. *That* seems to be, and is, a matter of *individual* records which an archivist of Graunt's generation might have conceived to be applicable to the family records of the Howards or de Veres, but how can any information of this kind be extracted from the contemporaneous records of deaths of a whole population? Graunt's answer was based upon the fact that if a population is stationary, the births balancing the deaths and the rates of mortality not changing, then knowing the age distribution of the deaths we can construct the order-of-dying-out. Possibly he did not realize that this condition is necessary as well as sufficient, and that an order-of-dying-out cannot be deduced from a summation of deaths unless the population is stationary in the above sense—which, by the way, is not the same thing as non-increasing\*—because he applied the method to London although the population was probably increasing and certainly not stationary in the special technical sense. But the step he took was a very important one and led to the development of a branch of vital statistics which for over a century was of much more practical value than any medical exploitation of his methods and results. Our practical-minded countrymen were quick to see that if one had a reasonably accurate order-of-dying-out, or, to give it its usual English names,

\* A population may not be increasing, the annual deaths may balance the births, and yet it may not be stationary in the required sense, for the death rates at ages may be varying, so that the age composition is not stable. Under those circumstances an accurate life table cannot be constructed by summation of deaths.

Table of Mortality or Life Table, the purchase and sale of contracts of life assurance or of annuities upon lives might be brought out of the class of mere gambling transactions and into the field of legitimate business operations. That life tables might be of value to the student of preventive medicine was hardly realized by anybody until Farr emphasized and perhaps over-emphasized their importance from that point of view. The vital nature of the assumption involved in the construction of a life table from deaths alone was realized by Graunt's immediate successor, Halley, and probably by others, even including Price, but Price, in constructing his famous Northampton Table, failed to guard against the errors involved when the method is applied to an increasing population, as did, indeed, almost all the eighteenth-century computers. It was only at the beginning of the nineteenth century that Milne constructed a life table upon correct lines which came into use. That Graunt's table was faulty, and also the tables of so many of his successors, does not mean wholly or even principally that he or they were bad reasoners. The fallacy of a life table made from deaths alone, when the population is increasing, if not intuitively obvious, does not require much reflection to discover. Graunt, who first pointed out how heavy was the mortality of childhood, would not have failed to notice that in an increasing population the sum of the year's deaths at all ages must give too small a denominator for the large numerator provided by that year's deaths at ages under one. But neither he nor his English successors for more than a century had any means of determining what should be the denominator, so that neither he nor they *could* base a life table upon rates of mortality at ages. At the worst they can be reproached with never having speculated as to the order of magnitude of the error involved. Perhaps it may not be too cynical to suggest that those who were interested in the sale of insurances upon lives rather than in dealing in annuities may not have been too anxious to replace tables of mortality which *overstated* the rates.

Although Graunt's most important discoveries were concerned with mortality as a function of age and locality, he by no means neglected a very important branch of medical statistics, viz. the criticism of sources. He was not a medical man, yet he saw and avoided pitfalls which a very accomplished medical man a century

later plunged blindly into, those pitfalls which consist in taking a new name for a new thing, or in supposing that what is not recorded does not happen. When Graunt found either a new name in the Bills or a large increase under an old heading, he would inquire whether the "new" disease or the suddenly increased disease might not have been lying hidden under other names, and would only accept an increase as genuine if no explanation on these lines were possible. Had the younger Heberden been as good a critic, the mythical decrease of dysentery in London would never have passed current. It is perhaps hardly necessary to say that Graunt recognized that the recorded mortality from syphilis was derisory. A number of mistakes have been made and published by even more recent physicians than Heberden the younger which Graunt could not have made.

As I am not writing on demography I do not propose to dwell upon the ingenuity with which Graunt used his scanty data to reach probable conclusions as to the size and rate of growth of the population. We are concerned only with epidemiology. I do not wish to enlarge upon the obvious. A reader will probably regard it as self-evident that when the problem is to determine how sudden prevalences of illness arise, to formulate the laws describing their emergence, we should start with a good working knowledge of how the average fluctuations of mortality are related to the age and sex composition of the population, to meteorological variations, and to other presumptive environmental factors of the situation. That, we have already seen, was Hippocrates' point of view; since, as Sydenham remarked, human life is not long enough for one man's experience to provide him with all the required particulars, it seems a plain deduction that some pooling of the experience of all and some universal notation for recording the data are required, and that the universal language of statistical arithmetic is such a notation. So, finally, it would seem that a vital or medical statistical system, codifying experience, is a necessary prerequisite of epidemiological research.

This, as I have said, probably seems almost self-evident, and I have already rather more than hinted that the failure of the Greeks and of such men as Ballonius or Sydenham to provide epidemiological doctrines which had much pragmatic value was because they had no such codification of data as Graunt began

to provide. But the more subtle-minded may object that all this is a trifle *too* obvious. Graunt's book was published in 1662; among his contemporaries—even without including Sydenham—were able physicians, and in the next hundred years there were many members of the profession of first-rate talents and a few men of genius. Again, the theory of statistical methods and the practical application of one of Graunt's methods occupied much of the time of some of the great masters of exact science: of Halley, of de Moivre, of the Bernouillis, and several others. Yet with only two exceptions no medical man in the eighteenth century in England seems to have attached any *epidemiological* importance to the line of research opened by Graunt. Take, for instance, the edition of Hippocrates' epidemiological treatises published by a Dr. Samuel Farr in 1780. This Farr was not, like his namesake, a genius, but he was a respectable member of our profession, an F.R.S., and something of a scholar. One finds neither in his preliminary dissertation nor in his elaborate notes the most distant allusion to medical statistics; years before his time Graunt's book had been republished, the Bills of Mortality down to 1752 collected, and some interesting calculations from the data made. This latter publication—which was financed by the great clinician William Heberden the elder—I reckon one of the two eighteenth-century English contributions to medical statistics. The other, also inspired by Graunt and also printed more than a quarter of a century before Farr wrote, is Dr. Thomas Short's *New Observations*. Short, who was a professed epidemiologist (another treatise of his, more directly concerned with epidemics, is alluded to with no great respect by our greatest epidemiological historian, the late Charles Creighton), made a determined attempt to define arithmetically the characters of healthy and unhealthy districts, the influence of soil, the succession of sickly years, and many other points of interest to medical as well as demographic students. Samuel Farr alludes to none of these things. The only way in which he differs from the ancient writers is in, not very happily, seeking to derive from the current chemistry of the time explanations of the mysterious properties of the atmosphere in generating epidemics. If the foundation Graunt laid were really of importance, it is strange that the medical profession should have ignored it so consistently.

Part of the explanation, the discreditable part, is, as always, easy to find. Dr. Arnold Chaplin is right in deploring the amount of time eighteenth-century doctors spent writing and speculating in their studies instead of reading the book of nature, and there is no reason to suppose that eighteenth-century doctors were any more enthusiastic arithmeticians than their great-great-grand-children.

But intellectual laziness and love of theoretic systematizing are not the only explanation of their attitude. There is another, viz. that the *kind* of information which must be synthesized to form a rational epidemiological system cannot, at least could not then, be expressed in columns of figures, that one must depend upon one's own experience, for it is impossible to make another man's experience one's own, as all parents discover.

Whether this be a universal truth, we must consider later on; it was certainly true in the eighteenth century. Then, I think, one had to face these epidemiological alternatives:

(1) Frankly to recognize that general epidemiology was too difficult an undertaking and to seek out the proximate causes of prevalences; be Browning's low man.

(2) To set up as a natural historian of epidemics and annalist, with a sort of sporting hope that Sydenham was wrong and that the life of a man *was* long enough to solve the great problem.

(3) To persist in speculation on respectable classical lines.

The inquisitive, philanthropic, energetic type of man chose the first; the meditative, naturalist type the second; the ordinary bookish man the third. Pringle, Lind, Percival are examples of the first, Huxham and the elder Wintrincham of the second, and Samuel Farr of the third species. So far as their literary survival to later times is a measure of success, there is no doubt which was the successful alternative. Pringle, Lind, and Percival are still well remembered by those who have but a hazy recollection even of Huxham and none at all of any of the Samuel Farris of the eighteenth century.

So that perhaps we should reach this conclusion about Graunt's *epidemiological* importance. We should agree that without his basis there can be no pragmatic epidemiology, but doubt whether with the help of descriptive statistics alone, even when elucidated

by the most subtle and beautiful of algebra, the general problems of aetiology which Hippocrates and Sydenham formulated can be solved.

That conclusion was reached, at least implicitly, in the eighteenth century, and before its end we entered upon another epoch. There remained some of the old school who hoped to solve the great riddle by sheer brain power, but there began to grow up a new school with something of the philosophy of Bishop Blougram; people who said, Let us ignore this riddle, perhaps it *has* no answer, and confine our efforts to doing first things. By this they meant the study of the obvious concomitants of over-average sickness and the ascertainment of whether their removal or modification affected the prevalence of illness. Of course philanthropists and keen administrators had acted in this way long before the end of the eighteenth century, but the change of intellectual atmosphere, associated with a demand for more precise information, is only noticeable at the end of the century, and such a man as Percival of Manchester was typical of his age.

Near the turn of the century one finds evidence of a revival of interest in medical statistics, exemplified by such monographs as those of Heberden and Woolcombe, and before the coming of William Farr a specific treatise on Medical Statistics was published by an academic physician. The author of this book, Francis Bisset Hawkins, whose long and useful life extended to the time of some senior contemporaries, hoped that his essay, published just a century ago, might become "one of the early milestones on a road which is comparatively new, rugged as yet and uninviting to the distant traveller, but which gradually discloses the most interesting prospects, and will at length, if I do not deceive myself by premature anticipation, largely recompense the patient adventurer."

Of epidemiology in Sydenham's or Farr's sense not a word is to be found in Hawkins' book. But there are frequent instances of the use of the statistical method purporting to demonstrate the effects of environmental improvements. Thus we read: "The mortality of Manchester was, about the middle of last century, 1 in 25; in 1770, 1 in 28. Forty years after, in 1811, the annual deaths are diminished almost beyond belief to 1 in 74; but the improvement does not stop even there, for in 1821 they appear

garden she was not big enough to reach the key which unlocked it. When she could reach the key she could not go through the door. So here we have a large experience placed at our disposal; it is divested of individuality so we are not tempted to follow personal issues: we must treat it epidemiologically and not clinically. We can reach the key and unlock the door, but we cannot go through it, because we are too big—swollen with wind the enemy will say. Hippocrates did not see as many people suffering from pneumonia in his whole lifetime as we can obtain statistics of, thanks to Farr, in ten minutes. But we are not synthesizing *our own* experiences of illnesses, we are not even dealing with the experiences of other men, but only with a codification of particular inferences these men drew from their experiences. We are judging a case on hearsay evidence at two removes. Some very able men doubt whether the statistical method, even when fairly and accurately employed, can ever deduce from the codification of opinions “laws” of epidemiological happenings.

Farr was quite conscious of all this—competent medical statisticians have nothing to learn from their critics about the weaknesses of the statistical method; in their polemics, and they are very polemical folk, they are usually engaged in trying to prove merely that accurate statistical methods are at least better tools than inaccurate ones. One will find that in his epidemiological work Farr dealt mostly with problems for which the data were least likely to be misleading. Stone-dead has no fellow, says the proverb; there is not much doubt about the *fact* of death, and the most sceptical appraiser of statistics is not likely to deny that for the measurement of the rate of mortality, *sans phrase*, civil registration in England and Wales did give the analyst an overwhelming advantage over his predecessors. More than half of Farr’s enduring work is on that plane. When he left the general death rate and dealt with the specific rates assigned to particular alleged causes of death his inferences are always cautiously drawn.

Farr’s direct contributions to the study of epidemiology are not very numerous. Upon the general problem he adopted early that sceptical attitude which, I have suggested, became fashionable when he was a child. “Epidemics appear to be generated at intervals in unhealthy places, spread, go through a regular

course, and decline; but of the cause of their evolutions no more is known than of the periodical paroxysms of ague." That was written in the Second Annual Report in 1840. In later life (particularly in the Thirtieth Annual Report), influenced by Darwin and Pasteur, he wrote on the *contagium vivum*, but I do not think that his views were really in advance of those of Fracastori, and his emphasis is always upon "practical" measures. Although a believer in specific immunization, he wrote: "It is, however, by no means proved that the general mortality under unfavourable sanitary conditions is much reduced by rendering a child insusceptible of one type, while he remains exposed to all other types of zymotic disease."

That is the language of a sensible man—it would have been impossible to persuade Farr that prophylaxis by inoculation is anything but a *pis aller*—but throws no light upon the genesis of epidemics. But although he threw no more light than Sydenham upon the secular evolution of epidemics he made a valuable contribution to the theory of the immediate evolution of particular prevalences. A sentence later than the words I have quoted from his Second Annual Report he continues: "If the latent cause of epidemics cannot be discovered, the mode in which it operates may be investigated. The laws of its action may be determined by observation, as well as the circumstances in which epidemics arise or by which they may be controlled." He then illustrates upon the deaths from smallpox in the epidemic of 1838-9 the regularity of decline of the mortality. In this particular case he took for his "law" the hypothesis that the second differences of the logarithms of the successive quotas of deaths should be constant, or in other words he supposed that in an epidemic the deaths in successive units of time will increase regularly to a maximum and then decrease at the same rate, so that the graph of deaths plotted as ordinates on a time axis would be a bell-shaped curve, the equation of which would be the so-called "normal" or Gauss-Laplace function. The late Dr. John Brownlee, who first directed the attention of contemporary epidemiologists to Farr's work in this field, showed that Farr here probably reached a first approximation to the truth. Although we are still very far from being able to classify epidemics by means of mathematical criteria, notable advances have been made; Brownlee

himself and Sir Ronald Ross have since pushed further into the territory entered by Farr more than ninety years ago.

Farr's work was done in his office or study, his duty did not take him into the world of men and women. It might have happened that his researches, like those of Graunt, would make no appeal to the members of our profession who had actually to treat sick men or to cope with the results of epidemics. The former class *were* very little moved by Farr's writings (which hardly any of them read—their successors pay equally little attention to the writings of Farr's successors), but the latter class were a good deal moved. After the establishment of the General Register Office, to a slight extent perhaps in consequence of the revelations of apparently preventable mortality that Farr made, still more because of the public feeling created by severe epidemic visitations (cholera), a State health department was organized and again providence was kind to the English. A medical man of first-rate ability was put in charge. That man was John Simon. The *intellectual* relation of Simon to Farr has a faint analogy to that of Petty to Graunt. As a scientific thinker, Farr was greater than Simon. Simon had none of the curious sagacity in perceiving the general truths at the back of statistical ratios which is the glory of Farr, as it was of Graunt; Simon used statistical evidence always pragmatically and sometimes tendentiously. But Simon came to his task with much more knowledge of the practical side of his profession than Farr had had either the opportunity or perhaps the inclination to acquire. He was a good judge of men, and from the first he was clothed in more personal authority than Farr ever attained. Simon gathered round him a band of very able assistants, several of whom were quite first rate, and the series of reports produced belong to the classics of the medical profession.

None of these reports—to the best of my knowledge—throws any light at all upon epidemic constitutions, they move in the pragmatic sphere of work of Percival and his contemporaries. But, against the general background afforded by knowledge of average rates of mortality, by using simple methods of statistical induction and common sense, the authors were able to make the *correlation* between neglect of ordinary cleanliness and outbursts of horrifying illness obvious to all men. Life is short,

one cannot be expected perhaps to read much of this literature. I select as an example of Simon's technique the epidemic of typhoid which occurred at the village of Terling in Essex in 1867.

The report on the field investigation itself by Thorne is a model of interesting presentation. One has first a vignette of this hamlet of very poor labourers—"socially there is nothing which can tend to raise or elevate the people; no middle class exists for them to imitate, or to which they can aspire to rise; there is almost a complete gap between the few wealthy residents and the poor labourer." Attention is directed to the fact that "hardly a well-built man is to be seen," and that an "extraordinarily large number of them are the victims of phthisis and scrofula." Then the squalor of their environment, the masses of filth in proximity to the shallow, uncovered wells from which their drinking water is drawn, and the state of domestic overcrowding are set out. Then we have an account of the epidemic itself. "Terling was now completely panic-stricken, and the moral effect of the tolling of the church bell at the death and funeral of the parishioners seemed so prejudicial not only to the sick, but also to those who still remained unaffected, that I thought it right to suggest to the vicar the immediate discontinuance of the ordinary custom." Then we have a careful study of time-relations leading to the conclusion that the determining cause of the pestilence was the rise in the level of the surface water carrying means of contamination into the unprotected wells. Here is Simon's summing up of the findings and their lesson:

"The epidemic at TERLING, in Essex, was one of extraordinary dimensions. In that village of only nine hundred inhabitants, and for the most part within a period of two months, fully three hundred persons were attacked with typhoid fever, and forty-one of the number died. That is to say, the one preventable disease killed in that short time a larger proportion of the population than all causes of death put together ought to have killed there in two years. The conditions which rendered possible this most calamitous visitation of disease were, as in all our other experiences, conditions of local filth. At Terling such conditions were at their worst. Round what pretends to be the house-accommodation of the tillers of the soil in Terling (a scanty overcrowded supply of dwellings of the meanest description) every possible source of pollution for air and water was accumulated; the peculiarly porous soil which underlay all this filth was of course continuously absorbing it; the water supply of the population was derived from wells, most

of them sunk in that excrement-sodden sponge of earth; some ten days before the outbreak of the fever, after an extraordinary period of drought, a sudden rise in the water-level of the wells was observed; and this of course denoted a long-delayed scouring of that foulest soil into the water supply of the now poisoned population. The epidemic incidentally deserved, and received, for ulterior reasons, very particular scientific investigation; but my reference to it in this place is exclusively for practical purposes. The filth which did so enormous an injury to human life, existed under definite legal responsibility. The Nuisance Authority of the place (the Board of Guardians of the Witham Union) had most grossly neglected its duty."

We do not write like that nowadays. The aetiologically similar outbreak in 1921 which affected three hundred and ninety-seven persons, killing forty-five of them, in the district of Bolton-upon-Dearne, certainly revealed a less gross neglect, yet might have provoked Simon to a harsher comment than that of his successor, viz. that "it therefore behoves all public authorities who are responsible for our water undertakings to use every endeavour to ensure the purity and safety of their supplies."

It may be that the cut-and-thrust style of Macaulay is less effective than we used to think at school, and any third-year medical student could show that the *detail* of Simon's aetiology is all wrong, that "filth" does not give us typhoid. Yet the wrong items were added to form a correct total, and pragmatic epidemiology in its strength more than in its weakness characterized the mid-Victorian period.

This was the intellectual and moral atmosphere of epidemiology until bacteriology came into its kingdom. We must very briefly consider that side of our subject next.

#### RECOMMENDATIONS FOR FURTHER STUDY

The most accessible edition of Graunt's work is the collected *Economic Writings of Sir William Petty*, edited by C. H. Hull (Cambridge University Press, 1899). The *canard* that Petty wrote Graunt's book has been revived in *The Petty Papers* (London, 1927); a discussion of the new "evidence" will be found in *Journal Roy. Stat. Soc.*, 1928, Vol. 91, pp. 79 et seq. A guide to the eighteenth-century writers will be found in Creighton's *History of Epidemics in Britain* (Cambridge, 1891). Short, it may be remarked, was rather more important than Creighton implies. The work of Farr has never been brought together, although the volume edited by Humphreys and published with the title *Vital Statistics*

(London, 1885) contains a good deal of valuable and characteristic matter. The student *must* read at least the first seven or eight volumes of the Annual Reports of the Registrar-General (not at all a formidable undertaking, since the bulk of the volumes is tabular matter) and the Thirty-Fifth Annual Report, in order to comprehend the importance of Farr. Simon's writings are accessible in three volumes, two of Public Health Reports, one on Sanitary Institutions, published in 1887 and 1890. The reports of the Medical Department of the Privy Council, of the Local Government Board, and of the Ministry of Health should also be consulted.

## IV

### THE AGE OF PASTEUR AND GALTON

IN a footnote to the Second Annual Report of the Registrar-General—the report quoted in the last chapter—Farr said that “the hypothesis that the causes of epidemics are generations of minute insects transmitted from one individual to another, through the medium of the atmosphere, has been ingeniously put by Dr. Holland in his *Medical Notes and Reflections*. Henle, of Berlin, has supported the theory by new facts and analogies.” Dr.—afterwards Sir Henry—Holland was a very successful man in his day, but although the historian of the College of Physicians pronounced the *Medical Notes and Reflections* to be “a work pregnant with information and with thought,” and prophesied that by this book Sir Henry would be remembered in his profession, it is not likely to be reprinted. Henle’s essay *was* reprinted, in 1910, in the series of Medical Classics edited by Karl Sudhoff. This Henle was the anatomist Jakob Henle, whose name is familiar to all medical students, and the essay, his solitary contribution to epidemiology, is worth reading, but not better worth reading than a book published in 1546—a condensed translation of which is also included in Sudhoff’s series\*—and written by a Veronese physician, Hieronymus Fracastori, who secured immortality by coining the word *syphilis*.

Fracastori was the first man to make it seem probable that a *living* contagium capable of propagation might be concerned in the transmission of disease.

Of course he was not the first to notice that illnesses spread from person to person; that had been recognized much more than one thousand years before his time; nor did he even push his own arguments to their logical conclusion. Although he was satisfied that syphilis was usually passed on by contagion, he shrank from accepting that as a sufficient account of the epidemic spread in the early sixteenth century, for “it would have been impossible that the contagion, which in itself is a slow business and not readily conceived, should have spread in so short a time

\* The complete text with a translation was edited by Meunier in 1893.

over so great an area." But the logical distinction between his teaching and that of Galen is clear. Neither in Galen nor in any other ancient writer is there evidence that they looked upon contagion as anything more than the passing on from one person to another of an unchanged something; there was no question of an active part played by, or within, the recipient of the contagion—he was a mere conducting medium. Fracastori likened contagion in disease to the rotting of fruits in contact, to a putrefaction, and was clearly striving to express the idea of a fermentation—he actually used the illustration of the souring of wine. Seeds or germs were, he thought, conveyed from one person to another; and these germs, "which possess the property of propagating and begetting their like," were the essential factors of contagious disease. Hence the difference between poisoning and contagion. A poison can, indeed, destroy, but it cannot initiate a fermentation.

There is no evidence that Fracastori's reasoning had any influence upon contemporary epidemiologists. When almost three hundred years later Henle expressed the same ideas in the language then current he was certainly not plagiarizing the Veronese physician, nor did Henle's work suggest to Farr—who was widely read—that of Fracastori. No doubt Henle's brochure would have attracted as little attention as Fracastori's—it did not really attract *much* attention in 1840—had it not been that the experimental method was in full working order. Most men, and nearly all medical men, born in the last one hundred years are suspicious of "arm-chair" reasoning; what they want is experimental *proof*. You may, by deductions from admitted facts, make it seem probable that if a mouse is held under water for five minutes it will die, but if you wish to carry emotional conviction you must actually drown a mouse.

It may be that a logical genius might have deduced from the data of observation many of the consequences which have transformed the arts of medicine and surgery, both preventive and curative, since the days of Pasteur; it may also be that several, perhaps most, of the classical experiments upon which our knowledge is based were really quite inconclusive. But it is historically true that the perhaps delusive simplicity and cogency of these experiments were stimulating and led to great practical advan-

tages. The application of the experimental method, leading to the identification and description of the *materies morbi* in some of the most important of diseases, gave *practically* a death-blow to the epidemic-constitutional or pneumatist epidemiology. That is part of the reason why Creighton spoke of bacteriology with an indifference which was not affected; while Sir William Hamer has rarely let slip an opportunity of genial sarcasm at the expense of bacteriologists, and would perhaps be inclined to generalize a particular proposition of his own, viz. that "in dealing with bacillus carriers the opinion of the bacteriologist is oftentimes regarded as an absolutely final pronouncement, and a kind of mental paralysis overtakes the epidemiologist." I do not, of course, mean that there was any logical reason why identification of *contagia viva* should lead us to discard general epidemiological principles, even pneumatist principles, but that such was the *practical* effect of the discovery. An instructive illustration is the rise and decline of the fame of Pettenkofer. Pettenkofer was probably the only man in the nineteenth century in an important teaching post really to modernize—that is, to translate into modern notation, and test upon data and by methods not available to Hippocrates—the Hippocratic plan of research exemplified in the tractate on Airs, Waters, and Places. In doing this he threw a great deal of light upon some factors of epidemicity of typhoid fever and of cholera. His teaching, sometimes called the Buhl or the Pettenkofer-Buhl "law," of the relation between changes in the level of the sub-soil water and changes of prevalence of the typhoid group of illnesses was very valuable. One will find that the important writers on epidemiology who were active *before* the bacteriological school had become psychologically omnipotent, such writers as Haeser and Hirsch, speak of this work with the greatest respect. Now, except to a small group of mainly south German writers, Pettenkofer and his teaching are as obsolete as Galen. This is not because anybody has refuted Pettenkofer's arguments, which like those of most mortals are partly good and partly bad, but because nobody any longer was interested in the *kind* of argument which appealed to Pettenkofer. Some of us are entirely pragmatist in our philosophy and all of us are somewhat pragmatist, so it was natural that more energy should be spent in hunting germs to their lairs, destroying them,

severing their channels of communication, or, if that could not be done, immunizing the population against their assaults, than in "theorizing."

This change of attitude was, pragmatically, justified; its weakness is illustrated in a charming fable which I quote from the late Dr. F. G. Crookshank's paper on *First Principles and Epidemiology*.

"Several years ago an ingenuous police surgeon, investigating what he was told was a case of murder, found a bullet in the heart. This, he decided, and so told the coroner, was the *causa vera*, the *causa causans*, of the symptoms in this case of murder. Shortly after he went abroad to a war, and, honestly believing that war is but murder on a large scale, he investigated the appearance of many bodies; again finding bullets, he declared that bullets are the cause of war, as of murder. But in not every fatal case was the bullet of the same kind. Moreover, the occasional absence of bullets disconcerted him until he realized that he had once found gas poisoning the *causa vera* in a case of murder, and he therefore came to the conclusion that several wars here existed, side by side; each one *sui generis*, and boasting a different *causa vera*. He then proposed to end war by discharging other and like bullets and gases in a contrary direction, and found many who approved his plan as sensible. However, some pestilent and philosophic person told him that war was not the mere numerical exaggeration of cases of murder, brought about either by an exaltation in the virulence of bullets or gas, or by a diminution in resistance to these agencies: it was our name for a state of affairs that we conceive as brought about by the play and interplay of racial, economic, and other factors. He was told, moreover, that while undoubtedly various kinds of killing are elements of war as conceived by the historian and statesman, wars are not to be prevented, as he hoped, by avoiding persons who, in trams and in cinemas, carry bullets, or who project poisonous gas in public places. He was, however, unconvinced, and returned to England more settled than ever that the causal agents of wars are bullets (of various kinds, no doubt) and gases (of various toxicities, certainly), while the best hope of preventing war in future lies, not in talk about vague, racial, economic, or political conditions (which can only, he thought, at most be pre-disposing), but in devising some means of circumventing the *causae causantes*, bullets and gas!" (See *Proc. Roy. Soc. Med.*, Sect. Epidem., XIII, 1919-20, pp. 159 et seq.)

Positive results of bacteriological and cognate experimental research which are of direct epidemiological importance have been the working out of certain biological sequences, and the bringing to light of unsuspected dangers to health and means

to avoid them. It is also now possible to modify *and study* the level of herd immunity.

Each of these achievements we shall have to consider in particular cases. The first is, perhaps, best illustrated by the epidemiology of plague, the second and the third by our present knowledge of the epidemiology of the typhoid group. There should not be, at least amongst medical men, much danger that these achievements will be under-valued. I hope not to be suspected of under-valuing them when I say that although they have provided some of the material for the synthesis which must be made before we can formulate epidemiological "laws," they have no more sufficed than did the data of pre-experimental descriptive or even of "classical" epidemiology to describe either the secular variations of disease-prevalence or even the immediate course of an epidemic. Dr. Crookshank's fable is hardly a travesty of the meagre *epidemiological* philosophy which has grown out of laboratory studies.

It has been said that medical men now are far better technicians than their grandparents, but less liberally educated. There is in an unqualified proposition such as that a statistical fallacy. The average literacy of medical authors may be below the standard of a century ago, but a century ago men whose educational training was that of the general practitioner, the apothecary, hardly wrote at all; their grandchildren *do* write. It is certainly an evil that medical men whose mother tongue is English or German take no pains to use those noble instruments of expression intelligibly and precisely; that it is not a *necessary* evil is proved by the example of the French. But this is not a subject upon which an epidemiologist has any special claim to air his opinions. He has, however, the excuse that when, as in epidemiology, we have to describe very complicated and at present obscure phenomena we should at least try to avoid gratuitous obscurity and ambiguity by writing clearly and correctly.

A more vital criticism is that a larger percentage of our grandparents than of ourselves was capable of conducting an argument from general principles. The principles may have been false, but it is arguable that false principles are better than none at all, and certain that much current epidemiology is purely hand to mouth.

While the experimental method in medicine was marching from triumph to triumph, a rather different technique was being perfected which for many years hardly came within the purview of either clinical or epidemiological investigators. That was the "new" statistical methodology whose greatest hierophants have been Lambert Adolphe Quetelet, Francis Galton, and Karl Pearson. This is not the place to describe, even in outline, the triumphs and the failures of that new movement, devotees of which have spread over the whole world. I permit myself only to say this; a cynic who has skimmed the pages of the bitterly controversial writings of the existing sects of statisticians, or even of the "superior" modern criticisms of the work of the three great men I have named, should, before passing judgment, ponder these facts. That the pioneers had to pass through years of ignorant and sometimes dishonest misrepresentation, and that those who, now the battle is won and biometry and statistics become "respectable," depreciate them and harp upon their errors, owe their very existence in a scientific sense to the pioneers whom they depreciate. Much bitterness, even some controversial unfairness, is to be forgiven in great men who have borne the burden and heat of the day.

The first impact of the new statistical *organon* upon medical science was purely destructive. The biometricians did not indeed test medical reasoning by resort to first principles—the most effective criticism of the statistical methodology of the English school is that its outlook has been too largely empirical, and that methods of analysis were introduced and widely employed without sufficient attention to the limitations imposed by the assumptions involved—but they did very conclusively show that some medical inferences drawn from numerical data simply did not follow at all from the data, and that a great many more were merely consistent with the premises but no more consistent with them than quite different conclusions. To put it shortly, it was demonstrated that conditions necessary for the adoption of various hypotheses were frequently—in fact usually—believed by our profession to be also sufficient. It would be asserted, for instance, that if five guinea-pigs out of ten died when treated in such-or-such a way, while eight out of ten "controls" died, *therefore* the treatment had some effect. It would be retorted that the facts

were *consistent* with that hypothesis, but also consistent with the *hypothesis* that the treatment was wholly irrelevant, *and*—this is of course the vital point—some numerical appreciation of the probability of reaching the observed result on the hypothesis of “chance” was provided.

At first, partly because the simplest hypotheses about “chance” events are usually illustrated on bags of balls or tosses of coins, the experimenters vehemently denied the relevance of the criticism, retorted that experimenting in a laboratory was very different from and more sophisticated than tossing a penny, and usually ended with a neat reference to the unpracticality of “mathematics.” As, however, it was not difficult to show that while it was certainly true that tossing a penny or dipping into a bag of balls was not the same thing as keeping guinea-pigs, treated and untreated, numerical appraisements based on these hypotheses were, on the whole, more favourable to the cogency of the experiment than deductions from any *other* plausible hypothesis, this line of defence has been abandoned by most workers, and, if anything, too much weight assigned to calculations of “significance.”

Similar controversies arose over the interpretation of the data of human experience. There the defence was that medical statistical data were too rough for it to be appropriate to apply “refined” mathematical tests to them. This defence had, however, decidedly less plausibility than the analogous defence of the laboratory worker. The experimenter could, and logically can still, argue that we know so little of the “universe of discourse”—the frequency distribution, let us say, of deaths in an infinite number of sets of ten guinea-pigs left untreated—that we *cannot* compute arithmetical chances, and can absolutely refuse to reason statistically at all. In practice, of course, he does always reason statistically, but in theory he need not. The field epidemiologist or public health officer *had* to reason statistically, and his rejoinder to the biometricians forced him to take up the logically hopeless position that one could find truth more easily from rough statistics roughly handled than from rough statistics carefully handled. This was clearly absurd, but behind it was a really cogent unexpressed argument. The administrator and field observer *did* fear that those who elaborated and delighted in methods of analysis

would come to believe that, given a sufficiently refined method of investigation, truth could be elicited from *any* data, however inaccurate or biased. Very able mathematicians, Condorcet and even Laplace himself, *had* believed that, and it is probable that such a belief greatly hampered the development of medical and vital statistics in France. Why *should* one bother to collect more data if a clever man can find truth without them?

I think the English biometrical school have made fewer mistakes of this kind than might have been expected. Indeed, many mistakes attributed to them—particularly with regard to the interpretation of measures of correlation—exist only in the minds of their critics. But a good many mistakes have been made—more of them abroad than in England—if only for the same reason that white sheep eat more than black ones. Most of these have been the work of those who used sharp instruments without knowing much about them, and, of course, cut very little but their own fingers. Some *have* been due to skilled analysts having insufficient knowledge of the data analysed, and these mistakes were much more serious because they tended to bring the statistical method into contempt.

Still, there is no real doubt that the present standard of descriptive accuracy is far higher, and the analysis to which the data are subjected far less superficial, than even twenty-five years ago. If one now asks whether this new statistical calculus, operating upon the very large quantities of raw material provided by the registrations of deaths, and even of case incidence, and by the hecatombs of animals offered up on the altars of experimental science, data which did not exist fifty years ago, has solved the problems of secular variation, change of type, method of spread, which the old pneumatists and other epidemiologists who lived before the deluge speculated about, the answer is quite unequivocal. *Not one* of these problems has been solved. As I think I shall make probable, we have not even solved much simpler epidemiological problems. We do not really know why the rate of mortality from tuberculosis has fallen as it has; we have not the least idea why scarlet fever, deadly fifty years ago, is now a relatively trivial cause of mortality.

There are two reasons for this. There is the obvious one that although the data amenable to the statistical method are numerous,

they do not cover a long period of time. Our own medical statistics are not yet a century old although—as a reasonably reliable body of data—they are almost the oldest in existence. A century is a very long time in the history of an individual, a very short time in the history of a population. The unit of epidemiology is not an individual but a population.

There is another even more important reason. All methods of analysis are selective; we must choose what to analyse. The very abundance of our medico-statistical information makes the choice of what to analyse difficult. Any intelligent man who has had a medical training can think of a hundred possible factors of epidemicity; but if he will investigate by the statistical or any other method, he must choose what seems to him the most plausible; he may be too ignorant to choose well, and, having chosen, may still be unable to isolate what he desires to study. One desires, perhaps, to measure the influence of domestic overcrowding upon the incidence of an infectious disease; one will find it impossible to discover groups *in pari materia* with respect to every variable save the housing conditions. One will have differences of age, occupation, economic status, perhaps of race and geographical situation. With the help of the method of multiple correlation some progress may be made, indeed has been made, but the journey is slow and difficult.

One is constantly faced with such a problem as this. The rate of mortality from respiratory diseases is highly correlated with the mean temperature of the air in the week before the date of registration of death. If one knows the mean air temperature of a week, one can form an estimate of the probable deviation of the death rate (from respiratory diseases) in the following week from the mean death rate, giving, on the average, better results, i.e. results nearer the truth, than if one did not know the temperature. But as a practical means of prediction an equation founded on this datum is not of much value. This is because mean air temperature is only one of many variables which will determine the rate of mortality. Let us, then, go a step further and bring in, say, the mean air temperature in the same week as that of registration of death and in the second previous week, i.e. use three “independent” variables instead of one for estimation; the result is not substantially better. The difficulty is that

owing to the high correlation of the three temperature factors among themselves, the actual increments to knowledge of really independent weight are small. This difficulty will hinder us even when we bring in other meteorological elements. We shall find that using all the plausible factors, meteorological and others, we are still unable to express variations of mortality in terms of variations of our related measures with an accuracy sufficient to satisfy even a lenient critic. *Part* of the explanation is that our statistical instrument is imperfect, that so far arithmetically manageable prediction, or regression, equations involving many variables have only been constructed upon the assumption that the equations will only involve the first powers of the variables. A more important cause of failure is that we have not chosen variables which while highly correlated with that which we desire to study are not highly correlated one with another. They *may* be there, their full record in Dame Nature's book, even if not copied into our official statistical records, but we do not know upon what page.

The statistician, however mathematical, has no magic spell which forces Dame Nature to treat him differently from other men. She always answers truthfully the question you ask her, not the question you *meant* to ask but the one you *did* ask.

Anybody, I think, who has patiently applied the statistical method to the complex data of recorded human experience in the hope of finding the laws of epidemic happenings will reach the same conclusion, viz. that he does not know enough of the elements of the subject to be fit to ask questions; that until he has studied something simpler than the palimpsests of human experience, it is hopeless to expect to learn much from them about the fundamental laws. That does not mean that their study is either uninteresting or useless—far from it—but it does imply that at present, with all our knowledge of detail, we shall not reach the general "laws" which Sydenham failed to discover.

#### RECOMMENDATIONS FOR FURTHER STUDY

For this period the reader's own general culture is, or ought to be, a sufficient guide. The only books which he might miss and ought not to miss are Udny Yule's *Introduction to the Theory of Statistics*, Tschuprow's *Korrelationslehre*, and Karl Pearson's *Life of Francis Galton*.

## EXPERIMENTAL EPIDEMIOLOGY

WHEN I originally prepared this book for the printer it included two chapters on the experimental study of epidemiology. Human vanity is irrepressible; it is quite impossible not to believe that what interests oneself must be exceedingly important. But one of the advantages of being a statistician is that the practitioner acquires a sense of at least arithmetical proportion. I cannot persuade even myself that what has so far been accomplished experimentally is really as important as the whole *corpus* of knowledge from Hippocrates to Farr (to which I gave two chapters), and therefore confine the discussion to a single non-technical chapter. Vanity yields the more gracefully, because I have been allowed an opportunity of discussing experimental epidemiology at greater length elsewhere. If this "popular" chapter interests the reader, he may be stimulated to read the Herter Lectures for 1931. One of the quatrains of Omar which we all knew by heart thirty years ago is:

*"Ah! Love! could Thou and I with Fate conspire,  
To grasp this sorry scheme of things entire,  
Would we not shatter it to bits—and then  
Remould it nearer to the heart's desire!"*

That sentiment appeals to the student of epidemiology. Epidemics behave so wilfully. The population will not stay put; all kinds of disturbing and—as we think—irrelevant factors destroy the simplicity and symmetry of the phenomenon. How much better it would be if we could mould a little epidemiological world of our own nearer to the heart's desire. That is the art of the experimental epidemiologist. He brings into existence a little world of his own, introduces into that world some sickness, and watches what happens. If he uses a short-lived animal such as the mouse, he has over the student of human epidemiology the following advantages: (1) He can in a year of study observe a succession of events which on the time scale of mice, who live not more than a thirtieth of the average of man's life, would be at least

equivalent to thirty years of human experience. (2) He can decide the numbers of entrants to his world. (3) He can decide what *materies morbi* shall be introduced and when it shall be introduced. (4) He can vary the environmental conditions of his flock.

These advantages are great. They must be paid for. The price is frank recognition that what we discover in this artificial world cannot without more ado be deemed a sufficient description of the world in which we live. It is always a difficulty of experimental simplification that we may have refined away just what is vitally important.

That is not the whole of the price; we must further bear in mind that the world we have made is only simple because we do not see its complexities. To us all Chinese look much alike, and no doubt to a Chinese all Englishmen look much alike. A herd of mice, perhaps, is only simpler than a town of men because we know men better than mice.

Because I do not repeat these cautions, it should not be inferred that I do not realize their gravity. To an ordinarily educated person, one of Einstein's monographs would be quite unintelligible; to a reader whose school days are far behind him, the prose of Cicero is as much a piece of magic (white or black) as a symphony of Beethoven. Working out examples in elementary algebra and doing exercises in Latin prose composition will not enable that reader to write like either Einstein or Cicero, will not even enable him to understand exactly how Einstein and Cicero were able to do what they did, but may give him some glimmering of the truth. Those who presume to judge either Einstein or Cicero without taking these pains will achieve nothing, not even the discovery of their own ignorant presumption. Experimental epidemiology has the same relation to human epidemiology that learning elementary algebra has to Einstein's work and writing simple Latin prose has to the compositions of Cicero.

Experimental work in England has been mainly concerned with two bacterial infections, one due to *Pasteurella*, and one due to *Bacterium aertrycke* and a virus infection *Ectromelia*. I shall deal with two questions only.

(1) When illness is introduced into a herd of mice and the population is recruited by the addition of uninfected healthy animals, what will happen?

The technique is as follows. A herd is inaugurated by bringing together a number of infected and healthy animals. It is maintained by adding daily to the herd a fixed number of healthy animals which have been subjected to a very rigorous process of quarantine, a process far more rigorous than entrants to any human herd, even the North American, have ever had to face.

This experiment has been carried out many times, both with herds in which pasteurellar infection and herds in which aertryckal infection has been implanted. In terms of the equivalent longevity of human beings, we have experience of centuries, and the teaching of that experience is this: The communities of mice exhibit the features of waxing and waning mortality, of epidemic peaks followed by quiescence, which the vital statistics of any human community record. On the whole, when the additions to the herd are numerous, the rate of mortality is speeded up; when the additions are few, the periods of quiescence are longer and the rate of mortality lower. A high addition rate means a high mortality rate. But so long as the herd continues to receive unsalted immigrants the illness continues. There may be long, very long, periods of quiescence. It may happen, since the herds are sometimes small, that the specific disease does actually pass out altogether. But the general sense of the results is that in a large herd the regular introduction of unprotected immigrants will confer a herd immortality upon the illness. It seems that in order to bring a herd illness to a definitive end, the introduction of new members must be wholly stopped. In other words, the doctrine that by guarding a herd, in which a disease has prevailed, against the importation of infected or of infection-bearing immigrants, we can control a herd sickness is, so far as concerns infections of this type, false doctrine.

This conclusion will not shock any experienced medical officer of health, or, indeed, any intelligent student of epidemiological history. Yet it is true that all countries probably waste much time and money in attempting the impossible, but the psychological explanation of that is simple. If we are in this position, that a particular herd illness either does not occur within our frontiers or within them is strictly limited to one or two foci and that its *materies morbi* breeds true, then, provided we can effectively close the frontiers against reimportation of *materies morbi* and

at once stamp out the internal foci, it is both theoretically and practically inevitable that the disease shall die out. But if success is not immediately secured, if the population becomes widely infected, then the method ceases to have any practical or theoretical justification. When, for instance, such an illness as swine fever or foot-and-mouth disease is confined to one or two farms, ruthless slaughter of the whole stocks, healthy and diseased alike, is a practicable policy. But when the disease spreads, the cost of slaughtering not only the affected animals but healthy animals on the same farms becomes prohibitive, so that the original policy is modified; only the prohibition of affected or infective immigrants is retained, and the contact of unsalted animals with the survivors of previous epidemics is permitted. The result is, as the experiment with mice would lead us to expect, that the herd sickness does not die out but reoccurs in the most perplexing way. As, however, a majority of the officials who in different countries report upon epidemics among farm animals cannot bring themselves to conceive that upon a farm or within a district wherein a scheduled disease once existed, and was afterwards officially declared to have ceased to exist, it could again start into life without a reimportation of *materies morbi*, these happenings must be explained by reimportation. We can always see a joke much more easily when it is against some poor foreigners rather than against ourselves. I advise an Englishman, therefore, to read the Dutch or German explanations of the recrudescence of foot-and-mouth disease and learn how the virus may be blown by the winds of heaven, or dropped on an island in the excreta of wild geese. A Dutchman might find explanations of the reimportation of foot-and-mouth disease to be found in English official documents equally bizarre. Indeed, the Dutch are perhaps ahead of the English in their scientific appreciation of the nature of the problem. Poels, writing in the report of the Netherlands' Royal Commission on the epidemic of 1918-19, remarked that "the possibility cannot be excluded that the infectious matter from a carrier which has been passed through one or more susceptible cattle is again in a condition to cause the disease in animals which have already passed through it and acquired some measure of immunity. It is conceivable that this may explain the recrudescence of foot-and-mouth disease without

importation of infective matter from elsewhere, under circumstances which produce on the uninstructed the impression of a spontaneous origin.”\* The results of experimental study of bacterial infection are consistent with this explanation. Our experience is that up to a certain point (*vide infra*) the longer animals survive in a community the lower the rate of mortality to which they are subject, but, sooner or later, a majority will die of the specific infection which has been the reigning malady in the herd to which they belonged. Whether, as Poels suggests, owing to an intensification of the virus by passage through a non-immune, or merely on the principle that the pitcher which goes often enough to the well will be broken, is not for the moment material. The discussion has proceeded on the supposition that closure of a frontier against importation of *materies morbi* can be made effective. If it cannot, and the learned epidemiologist Sticker, in his sardonic study of the measures taken to control cholera, has made it look very improbable that quarantine measures in cholera have ever had much effect or even have been sufficiently stringent to keep out specifically sick people, then *solventur tabulae risu*.

(2) The next problem is concerned with the *reaction of members of the herd to the conditions under which they live*. When we work out the rates of mortality in a herd tabulating by length of seniority, we find that at first the rate is very low. Very few animals die during the first few days' residence. The rate, however, increases, and within a few days reaches a maximum; then it begins to fall, and continues falling more and more slowly, never descending, in the cases of the *bacterial* infections we have studied, to nearly so low a level as the ordinary rate of mortality of mice *not* exposed to herd infection. Let us take as an illustration a herd of mice in which *B. aertrycke* infection existed and to which six healthy mice were added daily. This particular herd was under observation a whole year, and 2,226 mice were at some time members of the herd; 1,907 died in the herd, of these probably as many as 1,766 of the specific infection. The average daily population was a little more than 237. Only a few more than 1 in 1,000 died within the first day of membership; by the fifth day the proportion dying had mounted to  $7\frac{1}{2}$  per 1,000,

\* *Verslag van de Staatscommissie in Zake Mond- en Klauwzeer*, p. 28.

and by the fifteenth day was a little more than 60 per 1,000, the maximum rate. That is, of every 1,000 mice who had survived 15 days in the herd, more than 60 died before attaining a seniority of 16 days. From that point the rate fell, but never approached the figure of 1 per 1,000. For those of 25 days' seniority it was 51 per 1,000; for those of 30 days', 43 per 1,000; for those of 35 days', 28 per 1,000; for those of 50 days', 34 per 1,000. The rates oscillated above and below a level itself much above that which would measure the mortality of normal mice.

Up to a point these results are easily explained. Plainly mortality would at first be low, because time is required for the infection of the animals and for the evolution of the disease within those infected. We should also expect the rate of mortality to decrease from some maximum because not only will those particularly sensitive to the infection be destroyed, but those who pass through an attack will thereby presumably acquire some resistance. It is not, however, at all easy to decide which of these two mechanisms, the weeding out of the unfit or the acquirement of active immunity, is the more important, nor to account for the fact that the ultimate rate of mortality does not decline to anywhere near zero.

Some experimenters believe that the factor of selection is the more important, others—including Professor Topley and myself—believe that both factors are involved. We have, indeed, carried out a series of experiments which lead us to think that active immunization rather than mortuary selection is the stronger factor, but the details must be studied elsewhere. That the ultimate mortality, *mortality from the specific infection*, does not approximate to zero in our experience suggests that so long as the very unfavourable conditions implied by residence in a heavily infected herd recruited with non-immune stock are maintained, neither selection nor immunization can bring a herd sickness to an end. That is of course an extremely important deduction and must be strictly tested.

A sufficiently accurate way of comparing the resistance of mice to herd evils is to use an arithmetical summary which has been called the partial or limited expectation of life. If one watches each of a number of mice until death or the expiry of 60 days, whichever happens first, then, if 100 mice are in question, we shall

have a hundred scores, none of which can be larger than 60. The average of these scores will therefore be smaller than 60, and the higher the mortality the smaller it will be. When mice are kept under conditions identical with those of the experimental herds except that no infective material or animals have been admitted, the average calculated in this way is very nearly 57. Few mice die: mortality is usually due to fighting, a result of the high spirits which in human beings would no doubt find a vent on the dirt track or the football field. But when mice enter such a community as the one just described, where *B. aertrycke* is rampant, the average is as little as 27 days.

Now let us replace the unsalted immigrants by mice which have been artificially immunized against the reigning infection by the most efficient available laboratory technique. How do *they* fare? The answer is that their average score rises to 35 days; better than the unsalted, but very far from 57 days. This result was observed not only when the herd was recruited from both immunized and unimmunized mice, but when the entrants consisted only of immunized animals. In fact it seems that when we have to deal with herd sickness of *B. aertrycke* origin the disease will not die out even when unsalted immigrants are excluded; pre-immunized animals are sufficiently suitable pabulum. A herd maintained under those conditions will have at first a much lower death-rate than one maintained by the admission of unsalted animals, but the ultimate mortality in both communities will be approximately the same, and far above the level of a herd which has never been exposed to infection. This deduction is also, I think, congruent with human experience. There has seemed to be a certain conflict between the teaching of particular and of general experience with respect to the value of pre-immunization. One may have, perhaps, very convincing evidence that anti-typhoid inoculation has saved much sickness among troops, and that anti-smallpox vaccination has enabled doctors and attendants to face without harm immense risks of infection. It has been retorted that neither process has had much influence on the epidemiological history of enteric fever or of smallpox. I am not here concerned with the rights and wrongs of this discussion, but would merely point out that a method which is of enormous value to those exposed for a short time

to grave danger may be of little value in the long run to a community, an undying corporation, if always exposed to a risk. If in our experiments the pre-immunized and immunized mice were to be members of the infected herd for at most twenty-five days, and then were to be removed to relatively innocuous surroundings, the advantage of the former would be greater than the ratio of 35 to 27 measures. The trouble was a *continuance* of membership of a herd exposed to risk. The Victorian watchword that prevention, in the man in the street's sense, is better than cure is still not obsolete. It is a great deal better to provide clean houses and food than to pre-immunize people against the possible consequences of dirty houses and food, leaving the environmental conditions alone. It is fortunate for the world that pre-immunization against the typhoid group was not discovered in the days of *laissez-faire*; had it been, many more thousands would have died of typhoid than actually did. Eighty years ago it would have been hard to persuade the possessing classes to spend money on safeguarding water supplies if so cheap an alternative method of protection could have been provided.

A corollary to this would be that in *some* diseases immunization, at any rate the immunization due to passing through a natural attack, is wholly efficient. No doubt second attacks of measles do occur, but only as curiosities; from the herd point of view a solid immunity against measles can be acquired. Can we show anything analogous in a herd of mice? We can. Carrying out a herd experiment on precisely the same lines as those in which either *Pasteurella* or *B. aertrycke* was the *materies morbi*, but substituting contamination with the virus disease *Ectromelia*, it was found that when mortality declined from the maximum it fell very much nearer to the base line than in the bacterial infections studied, so that animals which have survived in such a herd more than sixty days did approximate much more closely to the mortality rate of still unexposed animals. To them, although members of a highly infected community, the infection had become almost harmless.

Why there should be this difference between these particular bacterial diseases and a particular virus disease is a question I cannot answer; if influenza be a virus disease, evidently there is no genetic distinction.

We have now completed the analogy between human and rodent herd experience, but, of course, only in a very broad way. We have shown that certain bacterial diseases of mice behave from an epidemiological point of view much like certain diseases of human crowds. The case, for instance, of aertryckal infection in mice is rather like that of the coli-typhoidal illnesses of man. The experiments with *Pasteurella* have some analogy with droplet infections of man, such as influenza or diphtheria. We may, from the preventive point of view, use the teaching of these long-continued experiments on mice as indications for practice. With the broad principle that it is quite futile to suppose that herd illnesses can be brought to an end merely by preventing the entrance of infected animals I have already dealt. I have also emphasized the fallacy of supposing that even highly efficient pre-immunization will be a satisfactory substitute for thorough-going sanitary reform. One of the still unsolved problems of epidemiology is to measure the balance of the several factors which determine the intensity of a crowd illness. In an infected crowd there will be at any moment groups and sub-groups of varying experience. A group composed of individuals clinically ill; a group of sub-clinically infected members; a group of individuals not infected at all. Upon the proportionality of these various groups (and sub-groups) the evolution of the crowd sickness depends. As yet we have no precise quantitative appreciation of the law of development. It does, however, seem probable that when the ratio of infective or potentially infective individuals to non-immunes sinks greatly, the progress of the disease is impeded. For instance, the sudden addition of a large number of non-immunes to an infected herd has a slighter effect in favouring the spread of the illness than the regular supply of smaller numbers. The addition of one hundred mice in one batch will do less to favour mortality than the drafting in of five mice a day for twenty days. A circulation of non-immunes seems to be a necessary condition of epidemicity. It follows that to break up a formed group must usually be sound anti-epidemic strategy.

Another interesting problem is as to the effect upon the evolution in a herd of epidemic sickness of breeding from stocks, members of which have, when experimentally tested, shown above

average resistance to specific infections. Some leading American experimenters like Dr. Webster attach great significance to this, and are inclined to think that a heritable general resistance is of very great importance. In England we have not yet sufficient experience of the fates of selectively bred animals to be able to offer an opinion. I would only say that the history of crowd illnesses in man can hardly be reconciled with a belief that in any genetic factor the solution of our difficulties can be found.

Similarly, but with rather more confidence because we have had a fair amount of experience, I should maintain a sceptical attitude towards the claims that diets rich in vitamins are capable of controlling in any real sense crowd illness.

If it be urged that, so far, experimental epidemiology has done little more than provide working models having a rough resemblance to the facts of crowd sickness as observed in human communities, I should not dissent, although I hope to have shown that something more has even now been done. But it is precisely the provision of suitable working models which is of importance. To revert to the metaphor I used at the beginning of the chapter, before we can presume to write essays in a foreign language we must learn the elements of its grammar. We have, it seems, learned some of the elements of this grammar now; we, or our successors, may hope to rise to original composition.

#### RECOMMENDED FOR FURTHER STUDY

*Epidemiology Historical and Experimental*, by Major Greenwood (Oxford University Press), 1932. The references in this brochure will be found useful.

## VI

### THE ARTIFICIAL IMMUNIZATION OF MAN

THIS chapter is concerned with topics which, in the strict sense of my definition of epidemiology, do not belong to the subject at all. But, since they can be discussed without detailed examination of particular facts—which fall to be considered in my chapters on the special epidemiology of particular crowd illnesses—and will certainly occupy much of the time and thought of readers in the public health services, practical convenience may justify what is essentially a digression.

In guarding or trying to guard the crowd itself or sub-groups of the crowd against sickness, we might adopt three methods, singly or in combination: (1) We might seek to breed a population naturally resistant to the particular sickness. (2) We might seek to render members of an unselected population, by artificial methods which can be lumped together under the convenient if unscientific name of vaccination, resistant to a *materies morbi*. (3) We might seek to shield the population from contact with or exposure to a *materies morbi*.

The first of these methods has never been voluntarily applied to man; the second, although of more recent application—at least in Europe—than the third, is now of a respectable antiquity. In the particular form of inoculation of smallpox it was practised in England two hundred years ago; the allied method of cow-pox inoculation has had a vogue of more than a century, and been more extensively used than any other prophylactic.

Honourable and able men have differed passionately in their opinions of these methods; vaccination against smallpox has been blessed and banned with theological vehemence; more modern applications of the principle have been defended and attacked with equal fury. The reader and I are of course greatly influenced by this emotional atmosphere. No intelligent person supposes that logic determines practical issues; some very wise men, such as Edmund Burke, have distrusted logic. But Burke and most other intelligent people thought it well to take stock of the logical aspects of a problem, and we must try to do so now. I hope

that in the last chapter I gave adequate reasons for doubting whether any method of immunizing could, single-handed, protect a crowd against the continuance of crowd sickness; at least I shall treat the problem before us on that assumption, and reduce it to these terms: What are the necessary and sufficient conditions for believing that an immunizing process diminishes the risk either of taking a disease if exposed to risk or of dying of that disease if it has been contracted, below the average measure of such risk run by persons not artificially immunized?

The solution of this apparently simple problem is beset with difficulties of two kinds, material and formal. In real life the material difficulties are almost insuperable, as we shall see; for the moment I postpone them, and suppose that the groups we have to compare are alike in all respects save two: they are alike in age constitution, sex constitution, race, social class, in *all* environmental circumstances; they differ only in respect of having been or not having been immunized, and, in the character we desire to measure, viz. their group reaction in face of the disease. On these assumptions our difficulties are only formal or analytical, viz. how the alleged advantage is to be measured.

In this ideal case the data are that  $n_1$  vaccinated persons have been exposed to the same risk as  $n_2$  persons not vaccinated, that  $m_1$  of the former and  $m_2$  of the latter have been attacked, or, alternatively, have died, and that  $m_1/n_1$  is smaller than  $m_2/n_2$ ; we may further suppose that neither  $n_1$  nor  $n_2$  is a very small number, and that the ratios of  $m_1$  to  $n_1$  and of  $m_2$  to  $n_2$  are also not very small. This means that the scale of our experiment runs at least to some hundreds, and that the attack (or fatality) rate of the unimmunized is of the order of 10 per cent or more. Since we are building a castle in Spain we can afford to be generous in our contractor's estimate, and may, temporarily, require another luxury, viz. that the attack (or fatality) rate upon unimmunized persons has been ascertained independently of this particular experiment from a very large experience of unimmunized persons *in pari materia* with the subjects of our experiment.

Anybody who has read an elementary textbook of statistical methods will say that the treatment is simple. If the immunizing process were really ineffective we should expect  $m_1/n_1 - m_2/n_2$  to be, on the average, zero, but we should expect "chance" to

induce fluctuations around that expected value; we should not, however, expect such chance deviations to exceed in magnitude two or three times the *standard deviation* of sampling, which is

$$\sqrt{\frac{p(1-p)(n_1+n_2)}{n_1n_2}}$$

where  $p$  is the attack (or fatality) rate on unimmunized persons in general. If the difference *does* exceed a fairly small multiple of this quantity, then it is improbable that if the immunized and unimmunized *were* equally liable to attack or death we should have found so large a difference between their reactions and easier to believe that the immunizing process was responsible for the difference than that the difference was a mere chance happening.

What we have really done is this. We have assumed that there is a perfect analogy between the comparison of samples of inoculated and uninoculated persons each individual of which is characterized by another marking, viz. the having or not having an illness, or alternatively the property of surviving or not surviving an attack of illness, and the comparison of two samples of counters in each of which every counter must be either black or white, drawn from a bag containing black and white counters in a known ratio, the draws being so made that the proportion of colours is unchanged (i.e. the bag contains an infinite number of counters, or, if not, after one counter has been drawn and its colour noted it is replaced before another is drawn).

On these assumptions the solution is exact—that is to say, the estimation of the probability that any particular difference between the proportions of blacks in two samples of size  $n_1$  and  $n_2$  is significant is accurate (provided the assumptions as to the  $n$ 's being large and the proportion of blacks in the bag not too small are fulfilled). Even at this stage there is a difficulty which is sometimes overlooked. In all mathematical reasoning, quantities are only great or small in relation to some other quantity. We are never really concerned with *absolutes*. One sometimes reads pseudo-mathematical arguments of the following kind. Data of the frequency with which a premonition of the death of some relation has corresponded with the actual occurrence of such death are compiled, and a calculation is given leading to the

result that the odds are millions to one against the concurrence being fortuitous; hence, it is argued, the concurrence was not fortuitous. Let us suppose—actually a very bold assumption—that the calculation is mathematically sound, i.e. that the probability schema (the assimilation of our case of inoculations to drawings from a bag of counters involves the choice of a particular probability system; in theoretical statistics the choice of the appropriate system or *schema* is one of considerable difficulty) chosen is applicable and the arithmetic has been done correctly; then all we have proved is that a very unusual event has come to pass. But the alternative hypothesis that the schema is *not* appropriate may involve improbabilities of thousands of millions to one. If we were playing cards for money with total strangers and our opponents held thirteen trumps between them several times running, we might be apt to infer that the cards had been stacked because the hypothesis, alternative to that of chance distribution, that we were being cheated had no strong *a priori* improbability attaching to it. Precisely the same sequence of events in a rubber among friends would lead to no such inference. The probability that an observed concurrence of premonitions and events is one in a million may well be a very large probability indeed in comparison with the acceptance, involved in the denial that the event *was* a chance happening, of the belief that our whole scientific *Weltanschauung* is false. There is a good deal more to be said about this, but the point I wish to make is that the computation of odds, even if the probability schema chosen is the right one, although a very important operation is not to be regarded as a decisive operation, a judgment against which no appeal can be entered. *If the probability schema chosen is the right one!* A hard saying! To begin with, there are certain formal difficulties. Suppose the *n*'s are *not* large and the ratio of, say, black counters to all counters *is* very small. Dropping the simplifying assumptions will compel us to use a different arithmetical measure, but it will present no difficulties which a competent statistician cannot overcome; I need not therefore discuss them, they are merely technical and can be learned from statistical handbooks. Dropping the assumption that we know the constitution of the bag of counters is also of minor importance. In practice we *must* drop that assumption, since neither the attack-

rate nor the fatality-rate of disease against which one seeks to immunize is effectively constant from year to year or from epidemic to epidemic. If we invent a bag the colour constitution of which is given by a pool of the two samples, our reasoning will for practical purposes, when  $n_1$  and  $n_2$  are large, still stand. We shall not be in danger of understating the probability that the samples are differentiated. But there is another, fundamental, assumption of the bag schema which is hard to justify. That assumption is that the drawing of one counter is wholly independent of the drawing of another; we are supposing that every counter in the bag has precisely the same chance of being drawn as every other counter. Were this not so—if the fact that the first member of a series drawn was black made it more (or less) likely that the next member of the draw would be black than if the first drawn had been white—then the mean proportion of blacks drawn in a series of samples would be as before, but the expected range of fluctuation about that mean would be widely different, and unless we can measure how much on the average one draw influences another we cannot determine arithmetically the extent of departure of the fluctuation from that of the standard case. But, when the question is not of the colours of counters, but of the falling sick of an infectious disease, it is plausible to suppose that the postulate of independence is unreasonable, that there is correlation between the individual events. For instance, to take an example given in Mr. Yule's classical *Introduction to the Theory of Statistics*, the variability of the annual deaths due to explosions in coalmines (data of 1887–1906) is about eight times the value to which the schema I am discussing would lead us. One obvious reason is that the "events" (deaths) are correlated: if an explosion is sufficiently serious to kill one person it is likely to kill others. This objection applies in principle to our data.

If we had before us a large number of sets of inoculated and uninoculated persons exposed to the same risk, we could investigate the extent of divergencies of the case from the simple one. If we have but the particular samples we are powerless, we can only guess. There is, on logical grounds, a good deal more to be said, but that would carry me too far. What I think is the *practical* conclusion is that such a test is not some infallible "mathematical" criterion, but a minimum test. If it fails to raise

a presumption of more than moderate improbability, we are not justified in inferring that the inoculated and uninoculated differ. If, on the other hand, very large odds are churned out by the arithmetical mill, we are *not* justified in roundly asserting that the betting is so-and-so many millions to one against the advantage of the inoculated being due to "chance." We must, every time, patiently explain the nature and limitations of our technique. A corollary is that when the comparison is not of attack-rates or of death-rates, but of fatality-rates, viz. ratios in the inoculated of deaths to attacked and in the uninoculated of deaths to attacks, the shortcomings of the method of assaying are less conspicuous, for it is less hard to believe that there really is no correlation between the individual events.

We are, then, to regard this process or any similar one as no more than a minimum test. If the result of a statistical experiment is approved by it, and, with the necessary reserves, we agree that the inoculated and uninoculated are differentiated, that is that the attack (or fatality) rate upon the inoculated is less than upon the uninoculated, it does not necessarily follow that the advantage conferred is of practical importance.

In estimating the probability of any result by the method we are discussing, both the numbers observed and the difference of incidence-rates are involved. In a numerically large experiment a difference between the attack-rates of the order of one in a thousand might be much less likely to be a chance fluctuation than a difference of the order of one in five observed in a smaller experiment. So in making a practical judgment we shall have to attend to these points. Suppose, for instance, that the attack-rates upon inoculated and uninoculated with respect to one disease were 20 per cent and 40 per cent respectively, with respect to another 1 per cent and 5 per cent. Then (assuming an adequate scale of experience and the fulfilment of the other conditions discussed above) in the former case inoculation might be said to save a percentage of twenty from attack, in the latter 4 per cent. The former confers a greater advantage, but, in another sense, the latter is more effective. In the former the attack-rate upon the inoculated is 50 per cent of that upon the uninoculated, in the latter only 20 per cent. In the former the method is more *advantageous*, in the latter more *effective*. In practice a method

might be highly *efficient* and yet its advantage might be too small to justify its introduction; we should have to count the cost. Those considerations are important in judging the practical value of, for instance, anti-smallpox vaccination if the prevailing type of the illness is mild.

These are some of the points one should consider when there are *only* statistical difficulties to conquer. It will be seen that, even then, the problem is not easy. Yet we have assumed that there are no other material difficulties. We have supposed that inoculated and uninoculated differ only, apart from the incidence of the character (attack or escape, death or recovery) we are assessing, in the quality of being or not being inoculated.

We have supposed that they all ran the same risk of taking (or dying of) the disease, were similarly housed and fed, were of the same age and sex; that, in fact, they differed in no *relevant* way except in respect of inoculation. I emphasize the word *relevant*. To determine whether a difference between the two classes is relevant to the object of study is sometimes a difficult, even an insuperable, problem.

Sometimes the existence of a relevant difference is obvious; two fallacies which have vitiated many published reports are easily described. One has data of the experience of inoculated and uninoculated persons collected over a wide range in space or time, and brings them together in a single statistical summary, which tells us that upon  $n$  inoculated persons the attack-rate was  $a$  per cent and upon  $m$  uninoculated  $b$  per cent. If  $n$  and  $m$  are large numbers, the kind of statistical test I have described may lead to arithmetically overwhelming odds in favour of the inoculated, yet this *a priori* inference might be quite wrong. It might be that in some of the experiments *neither inoculated nor uninoculated ran any serious risk at all*; if in these groups there were a *great majority of inoculated*, the final summary would show a great advantage to them. Suppose in one experiment there were 1,000 uninoculated with a death-rate of 50 per cent and 100 inoculated also with a death-rate of 50 per cent, while in another experiment there were 1,000 inoculated with a death-rate of 5 per cent and 100 uninoculated also with a death-rate of 5 per cent.

Summarizing, we should find 1,100 inoculated persons with 100 deaths, and 1,100 uninoculated with 505 deaths, an enormous

"advantage" to the inoculated group. No confidence should be placed in odds computed from such summaries.

If the protocols of the separate experiments are available, we can, of course, unmask any such fallacy.

Another fallacy of the same type, but not quite so obvious, is involved if comparison of attack-rates upon inoculated and uninoculated is made when the inoculation has been carried out during the course of an epidemic. The fallacy here is that the *time* risks of the two classes are unequal.

Suppose 1,000 persons equally exposed to the risk of catching some disease throughout a period of three weeks, that during each week one in a hundred is attacked, and that at the beginning of each week fifty people, *not already attacked*, receive injections of coloured water.

At the end of the first week there will be 950 uninoculated and 50 inoculated persons, and ten attacks will have been registered, 9.5 amongst uninoculated and 0.5 amongst inoculated. Stopping here we have identical attack-rates of 1 per cent. At the beginning of the next week we are left with 940.5 uninoculated and 49.5 inoculated who have not had the disease. Fifty of the former are now inoculated, so the numbers become 890.5 uninoculated and 99.5 inoculated; subjecting all to the 1 per cent attack-rate we have 8.905 victims amongst the uninoculated and 0.995 amongst the inoculated. Add up from the beginning and we have 100 inoculated persons, and 1.495 cases amongst them, 900 uninoculated with 18.405 cases, figures which give per mille rates of 15 and 20 respectively. At the end of the third week we shall, continuing the book-keeping, have 150 inoculated persons with 2.98 cases, and 850 uninoculated persons with 26.72 cases, rates per mille of 20 and 31. The essential fallacy is that those inoculated in, for instance, the third week formed part of the uninoculated exposed to risk in the first two weeks. The proper denominator is not a number of persons, but of person-time units, the time units belonging to any person must be distributed fairly. For this reason no data of inoculations performed during an epidemic are to be used unless sufficient details are given to enable one to allocate the time units of exposure to risk.

This second fallacy, although common enough, is not very likely

to deceive the student once it has been pointed out, but he must always be on his guard against the former error. During the Ministry of Health's study of the great pandemic of influenza, one wished to find out whether those who had had influenza in the summer of 1918 escaped more lightly in the autumn recrudescence than those who had not been attacked. One obtained, *inter alia*, data from four great public schools, Eton, Harrow, Haileybury, and Clifton, with respect to boys who had been exposed to risk in both summer and autumn terms. Here are the massed results:

Attacked in summer 825, of whom 121 (14·7 per cent) were attacked in autumn.

Not attacked in summer 1,323, of whom 602 (45·5 per cent) were attacked in autumn.

It would be a *very* stringent statistical test which did not lead to overwhelming odds in support of the inference that an attack of summer influenza conferred a substantial autumn immunity!

Here are the separate returns for the individual schools:

*Eton*.—393 attacked in summer, of these 29 (7·4 per cent) attacked in autumn; 360 not attacked in summer, of these 172 (47·8 per cent) attacked in autumn.

*Harrow*.—90 attacked in summer, of these 29 (32·0 per cent) attacked in autumn; 339 not attacked in summer, of these 258 (76·1 per cent) attacked in autumn.

*Clifton*.—162 attacked in summer, of these 22 (13·6 per cent) attacked in autumn; 289 not attacked in summer, of these 99 (34·3 per cent) attacked in autumn.

*Haileybury*.—180 attacked in summer, of these 41 (22·8 per cent) attacked in autumn; 335 not attacked in summer, of these 73 (21·8 per cent) attacked in autumn.

Haileybury is obviously not *in pari materia* with the other schools; there we have no suggestion of immunity. Further, the difference between it and the others is too great for it to be lightly dismissed as a random deviation. These data relate to a question which does not stir any emotions; had they related to some prophylactic experiment, one knows what would have happened. Those who, *on other grounds*—whether good or bad is irrelevant—had faith in the prophylactic would have spoken of the convincing evidence gathered at Eton, Harrow, and Clifton, and slighted the value of

the Haileybury experience. Those who had not that faith would have spoken of the convincing revelation of the inefficiency of injecting "filth" into clean bodies provided by Haileybury. Suppose this *were* a case of artificial prophylaxis, with protocols of statistical experiments under, so far as appeared, comparable conditions, and a medical officer had to advise his local authority whether to introduce the method in their area; what advice should he give? I think he must be guided by such considerations as these: If the risk or inconvenience of the method of prophylaxis is slight in comparison with that of taking the disease, the fact that in a majority of experiments a substantial advantage appeared to have been conferred ought to weigh heavily. But he must honestly say that he is going upon a balance of probabilities. It is always much easier to explain one's point of view by a concrete example, and so I will take the statements made in the official history of the Great War with respect to anti-typhoid inoculation. I choose these because, as will appear later, I think there is strong evidence for the belief that the inoculation is of value, so that in criticizing them I am not, I think, influenced by a reluctance to accept the conclusion.

The authors of this work,\* in their account of anti-typhoid inoculation, say almost at the beginning: "The progress of events during the five years of the war has proved conclusively that it is the best, most important, and successful means at our disposal for combating typhoid fever. Inoculation and systematic re-inoculation should be rigidly enforced in every army." This statement, if given as the conclusion reached by competent judges upon evidence too bulky to be published, would deserve respect; indeed, I should be inclined to accept it upon those terms. But unfortunately the statement follows that "the efficacy of prophylactic inoculation is shown in the following Table, taken from the official returns for the Western Front from 1914 to 1918." I reproduce the Table on page 88.

"It will be seen," continue our authors, "from this Table that the influence of protective inoculation on the liability to infection from enteric fever is undoubted, and equally undoubted is the very much lower case mortality in typhoid fever." If the reader studies this Table, bearing in mind the general logical

\* *History of the Great War—Medical Services. Disease of the War*, Vol. I.

TABLE I  
COMPARATIVE STATISTICS AMONGST PROTECTED AND UNPROTECTED MEN

Theatre of War	Year	Disease	Incidence per 1,000		Death-rate per 1,000		Case Mortality per 1,000		Number of Cases	
			Protected	Unprotected	Protected	Unprotected	Protected	Unprotected	Protected	Unprotected
France ..	1914	Typhoid	—	—	—	—	5·8	17·3	51	202
		Para A	—	—	—	—	—	—	—	5
		Para B	—	—	—	—	—	3·2	—	31
	1915	Typhoid	0·93	8·1	0·07	1·8	7·5	23·2	517	288
		Para A	—	0·4	—	0·003	—	0·7	—	281
		Para B	—	1·7	—	0·03	—	1·9	—	1,043
	1916	Typhoid	0·57	0·51	0·009	0·04	1·58	8·33	693	36
		Para A	0·21	3·19	0·003	0·05	1·56	1·78	256	224
		Para B	0·3	9·2	0·002	0·07	0·82	0·77	362	647
	1917	Typhoid	0·104	1·09	0·008	0·13	7·7	12·12	194	33
		Para A	0·07	1·12	0·000	0·03	—	2·93	139	34
		Para B	0·18	4·14	0·003	0·13	1·7	3·20	346	125
	1918	Typhoid	0·02	0·19	0·003	0·04	13·84	24·00	65	25
		Para A	0·01	0·04	0·000	—	2·7	—	37	6
		Para B	0·05	0·22	0·000	—	0·78	—	127	29

principles I have tried to develop, I think he will conclude that it proves hardly anything, being an example of the worst type of summarizing table. That it fails to satisfy a test of consistency is obvious. In 1915 the incidence-rate of typhoid upon the unprotected was 8.7 times that upon the protected, in 1916 the incidence-rate was rather greater upon the protected than upon the unprotected. That, however, is a triviality. It appears, working back from the incidence-rates, that in 1915, 542,900 were protected and 35,600 unprotected; in 1916 the round numbers are 1,215,800 and 70,600; in 1917, 1,865,400 and 30,300; in 1918, 3,250,000 and 131,600. That is, the unprotected formed roughly 6 per cent, 5.5 per cent, 1.6 per cent, and 3.9 per cent of the ration strengths in successive years. There is therefore an immense disparity of numbers. Further, the total incidence of cases is very small. But the incidence of typhoid is notoriously variable in time and space, so when we are dealing with millions of persons alleged to have been exposed to risk we naturally require some evidence that the risks were equally distributed, particularly when there is so great a discrepancy of numbers between the two groups. We might be dealing with a possibly equal incidence of infection upon the two groups when both were really exposed to risk, but the *summarized* attack-rate for one group would be watered down by the addition to the denominator of a large number of persons not exposed to risk at all. Of course we have no right to conclude that this is the explanation. *Prima facie* it is *not* probable that the proportion of unprotected in areas exposed to risk would be above the average; it is more likely that the proportion would be smaller, because one would expect the army authorities, who all believed in inoculation, to insist particularly upon its enforcement within danger zones. But we are talking about evidence given, not evidence which *might* have been given; in my opinion these unanalysed data are worthless as evidence. They add nothing to the presumption created by the data reported upon by the Committee of 1906. It is a pity that from this point of view the wartime experience has been wasted. But those who have had experience will know that to compile accurate statistics in wartime, even if one attaches importance to statistics, is not easy and will be lenient in their censures. It must be added that there is no reason to suppose

that the authors of the official report *did* attach any importance to statistics of this kind. They were probably much more impressed by an implicit argument which, although statistical, is statistical in a different way. The Table does certainly prove two propositions: (1) That for the first time in history a vast majority of the troops were "protected." (2) In comparison with some campaigns the incidence of diseases of the enteric group was trivial. The cogency of *that* argument does not depend at all upon the relative incidence of cases or deaths upon the protected and unprotected individuals; what is implicitly claimed is that a high level of herd immunity existed throughout the fighting forces, and that the heavy proportion of inoculated persons was the responsible factor. The discussion of that argument does not belong here; I can only refer to remarks made earlier in the chapter and shall have something more to say elsewhere. At present we are concerned with the inferences deducible from statistical experiments contrasting inoculated and uninoculated. If such an experiment *were* done during the war, the results have not, so far as I know, been published.

Have *any* experiments such as I require been made? Certainly none in which all the factors which *might* have influenced the result other than the inoculation were equally operative upon the contrasted groups. But I think there have been experiments where the *relevant* factors were constant. A case which, I think, is important is the now old story of the incidence of typhoid upon the 17th Lancers.\*

"The 17th Lancers were stationed at Edinburgh prior to their embarkation for India, and before Captain Luxmoore joined them in August 1905, Colonel Leishman visited the headquarters of the regiment in order to discuss the question of inoculation with the Commanding Officer. It must be borne in mind that in the case of these first units there was considerable difficulty in getting the men to come forward voluntarily as inoculation has been so long in abeyance and little response could be looked for in the absence of support from the Colonel and the officers of the corps concerned. In this instance the regimental authorities gave their cordial co-operation, and Captain Luxmoore after joining the regiment was able to inoculate 130 men out of a strength of 490 prior to embarkation.

\* *Report of the Anti-Typhoid Committee, 1912* (H.M. Stationery Office), pp. 61 et seq.

"The vaccine used in this instance was the 'new' vaccine, as the results of the experiments at the Royal Army Medical College had by this time shown that the earlier method of preparation diminished to a considerable degree the immunizing properties.

"The Lancers sailed in September 1905, and reached their station, Meerut, on October 4, 1905. They remained at this station during the whole of the three years during which they were under observation.

"As Captain Luxmoore remained at the station after the expiry of his three years' appointment, and was still in touch with the regiment, the report brings its history up to July 1909, a period of observation of three years ten months.

"*Inoculations.*—As mentioned above, 130 men were inoculated out of a strength of 490 before sailing. Very soon after reaching Meerut, indeed in the month following, a severe epidemic of enteric attacked the regiment, and the incidence of the disease being almost exclusively confined to those who had not been inoculated naturally proved of great help in the subsequent endeavours of Captain Luxmoore to increase the number of the inoculated. During the period of three years during which he was attached to the Lancers he carried out no less than 433 fresh inoculations and 263 reinoculations. At the date of the last return from the regiment, dated August 9, 1909, there were present 460 inoculated men out of a strength of 620.

"In addition to the number of men protected by inoculation there are always present a certain number of soldiers who have suffered from enteric fever in the past. In the case of this regiment, in particular, this group was a gradually increasing one, and eventually attained considerable size owing to the very large number of cases which occurred during the period of observation. This is a factor which to some extent complicates all returns of inoculation concerning soldiers, and it was partly for this reason that a limit of three years was fixed upon as the maximum period during which it was unlikely to interfere with the general statistical observations to any great extent. Whatever influence this has on the figures it was decided not to attempt a statistical record of it in the case of these units as it was particularly desired to keep them as simple and easy of interpretation as possible. Finally, it may be neglected the more safely as any influence which it might be shown to have on the figures would be to the disadvantage and not to the advantage of inoculation, since men who have had enteric in the past and who have never been inoculated are, in a sense, protected men, who go to swell the numbers of the uninoculated.

"However, in this case of the 17th Lancers, in which the number of cases of enteric has been much the largest of any of the twenty-four units, and in which, in consequence, the number of the men shown as non-inoculated in the returns comprises a larger proportion of men protected by a previous attack than in any other unit, Captain Luxmoore worked out the following Tables. In these it will be seen that he deals with averages and not actuals as regards the strengths. These averages

were obtained by adding together the number of days in the year for which each man was, as the case may be, protected by one, two, or more doses of vaccine, unprotected by inoculation, or protected by a previous attack of enteric fever; the result was then divided by the number of days in the year.

TABLE 2

AVERAGES FOR THE FIRST TWELVE MONTHS IN INDIA

Average Annual Strength, 562	Strength	Admissions for Enteric	Deaths from Enteric
Average number of men unprotected by inoculation or previous attack of enteric	373	64	11
Average number of men protected by one dose only .. .. .	33	2	0
Average number of men protected by two or more doses .. .. .	110	0	0
Average number of men protected by previous attack of enteric .. ..	46	0	0

TABLE 3

AVERAGES FOR THE SECOND TWELVE MONTHS IN INDIA

Average Annual Strength, 616	Strength	Admissions for Enteric	Deaths from Enteric
Average number of men unprotected by inoculation or previous attack of enteric	238	6	1
Average number of men protected by one dose only .. .. .	35	0	0
Average number of men protected by two or more doses .. .. .	287	0	0
Average number of men protected by previous attack of enteric .. ..	56	0	0

*"Incidence of Enteric.*—The disease appeared in the regiment within a few weeks of their arrival at Meerut, and sixty-six cases with eleven deaths had occurred in the period of one year from their arrival at Meerut.\* It will thus be seen that the regiment presented a marked contrast to that which has just been described, the Royal Fusiliers, inasmuch as it was attacked by enteric within a few weeks of the carrying out of the first inoculations, and a greater part of the incidence of the disease occurred within a year after inoculation. Another point of differ-

\* A detailed account of the greater portion of this epidemic, sixty cases, has been published by Captain Luxmoore in the *Journal of the Royal Army Medical Corps*, Vol. VIII, p. 492, 1907.

ence lies in the fact that in this regiment the 'new' vaccine was employed for the first time, as the experiments already referred to had been concluded shortly before the departure of the Lancers from England.

"The occurrence of the epidemic therefore afforded the opportunity of determining, to some extent, the value of the modifications introduced in the preparation of the vaccine and its protective properties in the case of men who had, presumably, reached the highest point of their immunization.

"The early effects of inoculation in the regiment may be readily appreciated by the study of the following Table, which records the results reported by Captain Luxmoore from the arrival of the regiment in India up to May 1, 1907, a period of one year and seven months. Under each date is given the total number of cases and deaths which had occurred in each group up to that date.

TABLE 4

17TH LANCERS—ARRIVED MEERUT OCTOBER 4, 1905

Date	Strength of Regiment*	Inoculated			Non-inoculated		
		Strength	Cases	Died	Strength	Cases	Died
December 4, 1905 ..	592	172	1	0	420	36	5
January 5, 1906 ..	614	174	1	0	440	46	6
September 30, 1906	680	258	2	0	422	66	11
December 30, 1906	676	396	2	0	280	68	11
May 1, 1907 .. ..	628	425	2	0	203	69	11

\* In the above returns officers are included in the strengths, in all other returns they are excluded.

"The above Table covers the period of the greatest incidence of enteric in the regiment, and there were only a few more cases during the remainder of the year 1907. In the following year, 1908, cases occurred at intervals throughout the year, and on December 30th, i.e. two years and three months since their arrival in India, the figures stood as follows (officers are not included, and the strengths are the actual strengths then present with the regiment and are not average strengths):

Strength of regiment .. ..	650
Number of inoculated .. ..	430
Number of uninoculated .. ..	220
Cases of enteric in inoculated men .. ..	13
Deaths from enteric in inoculated men .. ..	1
Cases of enteric in uninoculated men .. ..	95
Deaths from enteric in uninoculated men .. ..	13

"Although Captain Luxmoore's period of attachment to the regiment terminated on October 4th of this year he remained on duty at Meerut, and was therefore able to furnish later information as to the further incidence of the disease, and in the last return furnished by him on August 9, 1909, the results stand as follows:

*Résumé*

Strength of regiment .. .. .	620
Number of inoculated .. .. .	460
Number of uninoculated .. .. .	160
Cases of enteric in inoculated men .. .. .	18
Deaths from enteric in inoculated men .. .. .	2
Cases of enteric in uninoculated men .. .. .	96
Deaths from enteric in uninoculated men .. .. .	18

*Case Incidence*

Inoculated .. .. .	39.1 per 1,000
Non-inoculated .. .. .	600 per 1,000

*Case Mortality*

Inoculated .. .. .	11.1 per cent
Non-inoculated .. .. .	18.7 per cent

"In this regiment, therefore, not only has the incidence of enteric fever been exceptionally severe, but the ratio of the cases occurring in the inoculated to those in the non-inoculated stands, at the end of the three years and ten months' observation, at the remarkable figure of 1 : 15.

"From the case mortality in the non-inoculated it is evident that the type of the disease was of the average severity encountered in India, and apart from this the diagnosis has been verified as far as possible by agglutination work, and, during recent years, by blood cultures during the attack. As a result of the systematic attempts made to isolate the causative bacillus a certain proportion of cases of para-typhoid infection were encountered, but since these examinations were not found to be practicable during the first year of observation and both groups may therefore have included a certain number of such para-typhoids, the cases of this disease subsequently encountered have been allowed to remain in whichever group they occurred. In this connection, however, it must be borne in mind that the experimental work detailed in the earlier section demonstrated that typhoid vaccine had little or no protective effect against para-typhoid infections; the inclusion, therefore, of certain cases of this infection in the total of the cases occurring in inoculated men is unfair to inoculation. In the subsequent units such para-typhoid infections, as has already been mentioned, have been excluded from both groups when the evidence was complete.

"A few more points of interest emerge from a consideration of the details of the cases which occurred in inoculated men.

"The smaller degree of immunity conferred by a single dose of vaccine as contrasted with that resulting from two doses appears manifest, since no less than six of the whole eighteen cases which occurred in the inoculated were in men who had refused to have their second dose, and who, in consequence, had received only one-third of the amount of vaccine given to the others. This was especially marked during the first two years, during which the only cases which occurred in inoculated men, two in number out of a total of seventy-two during this period, were in men who had only had one dose."

Tried by any of the arithmetical tests I have mentioned there is no doubt as to the advantage, on paper, of the inoculated,\* but our greatest statistician, Professor Karl Pearson, objected *inter alia* that "the so-called 'controls' cannot be considered as true controls until it is demonstrated that the men who are most anxious and particular about their health, the men who are most likely to be cautious and run no risk, are not the very men who will volunteer to be inoculated; thus a spurious correlation may be produced between attack and absence of inoculation." The reader is quite as competent as I to assess the value of this criticism. I will only say that to me the objection seems less formidable than it would to a layman. If, in fact, the typhoid experienced by these troops were water-borne, and if, that being admitted, careful soldiers were able to boil their drinking water, if again there were evidence that volunteers for inoculation really were more careful in their personal hygiene than their uninoculated comrades, the objection would be fatal. But I have not found any evidence that a single one of these conditions was fulfilled. Were the typhoid of the soldiers conveyed by food fouled by flies or carriers, no individual action could have affected the issue. Further, an officer of the Indian Medical Service who attended my lectures many years ago told me that an investigation of the incidence of venereal disease upon the inoculated and uninoculated strengths brought out no significant difference, a result which, *if confirmed*—I have never had an opportunity of verifying

\* For such a test the data of Tables 2 and 3 should be used; these correctly compiled Tables show 70 cases for 611 man-years in the uninoculated state and 2 cases for 465 man-years in the inoculated state. Table 4 and the two summaries must, I think, be affected by the fallacy discussed on page 85 and exaggerate the advantage enjoyed by the inoculated considerably.

the facts—would be strong evidence against the assumption that the inoculated men were really more rigorous than their comrades in taking hygienic precautions. Hence, I should attach more weight to this evidence than Professor Pearson did. Similarly, I think the experience of the Sanitary Corps of the Greek army in the Second Balkan War (1913) rather impressive. The question was of anti-cholera inoculation. All the members of the Sanitary Corps had been inoculated before exposure to risk, only a minority of the combatants. Among 2,897 members of the Sanitary Corps there were 13 cases of cholera, among 114,805 combatants 2,192, an enormous discrepancy, one not, so far as appears, correlated with any difference of exposure to risk. The report, by Savas, is not complete enough to satisfy an epidemiologist, but I can discover no material fallacy in it. As Mr. Yule and I wrote when the report was recent history: "We know no more about the Greek Sanitary Corps than Savas tells us. They may all have been vegetarians, or non-smokers, or red-headed, and all or any of these things may render them less likely to contract cholera; but we do not see why objections which no sensible man would allow to influence him in the ordinary affairs of life should suddenly acquire scientific importance when the question is one of interpreting statistics."

I should be inclined to adopt a similar attitude towards the kind of indirect evidence which has impressed practically all trained statisticians in the special case of anti-smallpox vaccination. I mean the demonstration that the fatality of smallpox decreases as the extent or intensity of the dermal changes produced by vaccination increases. The *prima facie* interpretation is that *if* the local reaction is a measure of the efficiency of the immunization, the latter is negatively correlated with the rate of fatality. This obvious interpretation might be wrong. Certainly another variable—as Creighton pointed out—is the texture of the skin itself; if a hundred children were each vaccinated in identically the same way, the resultant cicatrices might, and probably would, all differ. Hence, it has been suggested that the rather elaborate statistical demonstrations of a correlation between area of cicatrization and fatality from smallpox amount to no more than a demonstration that smallpox affects differently different constitutional types. This *is* all possible. But we must

remember that: (1) Nobody *has* demonstrated that the kind of person whose skin reacts by severe cicatrization to an inoculation is less likely to die of smallpox than those less sensitive. (2) Plenty of people have demonstrated upon random samples that in general the wider the scarified area or the more numerous the punctures the greater the amount of cicatrization. In other words, in accepting the interpretation placed upon the statistical facts by Pearson, Turner, Brownlee, and others, we are accepting an interpretation which *may* be wrong, but which explains the observations most simply. In accepting the interpretation of Creighton we violate the practical rule of parsimony and substitute for the probable the possible. Why very able men, like Creighton, *have* accepted the less probable alternative is because they had convinced themselves on other grounds that vaccination was irrational. In this chapter I am concerned only with evidence of a particular class, so that these other reasons are irrelevant.

That ends what I have to say on the logic and arithmetic of measuring the value of artificial immunization. The actual technique of the assessments—the choice of suitable coefficients to measure the results—belongs to the practice of statistics and needs separate treatment. I will only add that when a whole series of comparisons between the attack- or fatality-rates of the two classes in different epidemics is available, further study is possible. This, however, involves more knowledge of statistical methods than I have assumed the reader to possess, and I doubt whether the data of human experience are sufficient (in point of quality) to provide a satisfactory test of any theory.

#### RECOMMENDATIONS FOR FURTHER STUDY

The arguments used in this lecture are based upon the considerations expressed in the following:

Greenwood and Yule. *Proc. Roy. Soc. Med.*, 1915, Vol. VIII (Section of Epidem. and State Med.), pp. 118–90.

Ministry of Health. *Report on the Pandemic of Influenza*, London, 1920, pp. 131–49.

Greenwood. *Journ. Roy. Stat. Soc.*, 1930, Vol. XCIII, pp. 233–70.

## VII

### PROCATARCTIC CAUSES—NUTRITION

WE have seen that the Greek men of science believed that ill health was the product of one intrinsic and two extrinsic cause-groups, viz. (1) man's temperament, (2) his diet and other habits of life, (3) an "atmospheric" influence. The last, which included far more than what we now call climatological or meteorological influences, cannot be intelligibly discussed in general terms. The first, which should include the whole body of facts concerned with the innate and hereditary qualities of man, is also unsuitable for merely general treatment, not because it is unimportant; on the contrary, it is very probably—as the Greeks believed—more important than either of the others, but because any account unaccompanied by a mass of detailed illustration must be trivial or dogmatic.

The second cause-group, although it, too, really needs a wealth of illustration, can, however, be examined with advantage before we pass to the consideration of special diseases. This, which used to be called a *procatactic* cause, and had better continue to be so-called because the usual equivalent, predisposing, ought etymologically to include the temperamental or constitutional factor, may be summarily described as habits of life. Eating and drinking and the way one spends one's time when not eating or drinking cover all human life. Without digressing far into special epidemiology, something not altogether vague can be said of each.

The modern study of nutrition has passed through two phases and is now in a third.

The first phase was quantitative and physical; the second biochemical. The third is a blend of both flavoured, perhaps, with a *souçon* of doubt whether we are quite so clever as we thought we were.

The actual pioneer of the measuring school was Santorio Santoro, but Lavoisier first enunciated clearly the doctrine which, in the view of most people down to very recent times, should determine a nutritional policy. In 1789 Lavoisier and Seguin

showed that the consumption of oxygen increased as the amount of manual work done increased. It seemed to Lavoisier, full of the enthusiasm of the pre-revolutionary epoch, something of a paradox that the poor manual worker who needed more food than the rich man actually got less. "Par quelle fatalité," he remarked, "arrive-t-il que l'homme pauvre, qui vit du travail de ses bras, qui est obligé de déployer pour sa subsistance tout ce que la nature lui a donné de forces, consomme plus que l'homme oisif, tandis que ce dernier a moins besoin de réparer? Pourquoi, par un contraste choquant, l'homme riche jouit-il d'une abondance qui ne lui est pas physiquement nécessaire et qui semblait destinée pour l'homme laborieux? Gardons-nous cependant de calomnier la nature, et de l'accuser des fautes qui tiennent sans doute à nos institutions sociales et qui peut-être en sont inséparables. Contentons-nous de bénir la philosophie et l'humanité, qui se réunissent pour nous promettre des institutions sages. . . . Faisons des vœux surtout pour que l'enthousiasme et l'exagération que s'emparent si facilement des hommes réunis en assemblées nombreuses, pour que les passions humaines qui entraînent la multitude si souvent contre son propre intérêt, et qui comprennent dans leur tourbillon le sage et le philosophe comme les autres hommes, ne renversent pas un ouvrage entrepris dans de si belles vues, et ne détruisent pas l'espérance de la patrie."

Five years later his countrymen gave the author of this warning a convincing demonstration of how little they had profited by it.

Although a Scottish contemporary of Lavoisier, Crawford, made and described similar quantitative experiments, Lavoisier had been dead fifty years before effect was given to his suggestions and Liebig gave a fresh impetus to such studies. The chemists of the mid-nineteenth century rectified Lavoisier's too simple conception that human metabolism was precisely analogous to the burning of a candle, but the comparison of the human body to a heat engine continued to be attractive, and Joule's discovery of the mechanical equivalent of heat simplified the quantitative treatment of the problem. One reached the position that Man was a machine, differing from non-living machines in this respect, that to keep the machine in repair it was essential that certain complex nitrogen-containing substances, now called proteins,

should be supplied and desirable that two other simpler chemical substances, carbohydrates and fats, should be furnished. Any work done by the machine must be covered by the combustion of one or all of these proximate principles. One might determine the optimum diet for different kinds of work by exactly measuring the use of energy by individuals subjected to precisely regulated conditions in a laboratory. This, however, could only be done in relatively few instances since the technique was difficult. Such

TABLE 5

## HEAT PRODUCTION AND WORK

*Observations of Benedict and Cathcart on M.A.M. pedalling at the rate of 68-72 revolutions per minute (inclusive)*

Work Done	Observed Heat Production	Mean of Observations	Number of Units of Heat Produced per Minute = 3.3415 (Number of Units of Work Done) + 2.4131
Calories	Calories		
0.47	4.01, 4.01	4.01	3.98
0.48	3.86, 3.88, 3.83, 4.13, 3.96	3.93	4.02
0.49	4.15, 3.94	4.05	4.05
1.19	6.73	6.73	6.39
1.20	6.65, 6.81	6.73	6.42
1.33	6.95	6.95	6.86
1.35	6.97	6.97	6.92
1.36	7.08	7.08	6.96
1.56	7.44, 7.66	7.55	7.62
1.57	7.87, 7.59, 7.53, 7.64	7.59	7.66
	7.64, 7.41, 7.51, 7.55		
1.59	7.56	7.56	7.73

experiments could be supplemented by arithmetical reductions to terms of calories, grammes of protein, fat, and carbohydrate of the dietaries of different social and economic classes. In the study of nutrition as elsewhere, Science was a Measurement.

In the last fifty years an immense amount of such work has been done, and its general standard of accuracy has been high.

Let us consider first the experimental studies. In one sense the relation between work done and energy used is a very simple one, in the same sense that the average increase of energy consumption for unit increase of work done is represented with very fair accuracy by the simplest of descriptive laws, the linear

relation. But even when one is considering an individual, the variation about the mean is large. Benedict and Cathcart published in 1913 a long series of exact measurements of the energy transformations of a trained cyclist pedalling a bicycle against a variable resistance at varying speeds. As appears from Tables 5 and 6 there is a fair agreement between the *average* heat production for different loads and that assigned by a linear relation

TABLE 6

## HEAT PRODUCTION AND WORK

*Observations of Benedict and Cathcart on M.A.M. pedalling at the rate of 98-102 revolutions per minute (inclusive)*

Work Done	Observed Heat Production	Mean of Observations	Number of Units of Heat Produced per Minute = $3.61225$ (Number of Units of Work Done) + $3.7543$
Calories	Calories		
0.55	5.59, 5.28, 6.03, 5.60, 5.64	5.63	5.74
0.56	5.72	5.72	5.78
1.35	8.72	8.72	8.63
1.62	10.15	10.15	9.61
1.63	10.88	10.88	9.64
2.05	11.24	11.24	11.16
2.06	11.30	11.30	11.20
2.07	10.82, 11.21, 11.43, 10.91	11.09	11.23
2.08	11.19	11.19	11.27
2.09	10.98, 11.65, 11.74	11.46	11.30
2.10	11.26	11.26	11.34
2.11	11.13, 11.15, 11.39, 11.35	11.26	11.38
2.12	11.29, 11.35, 11.03, 11.29	11.24	11.41

between heat production and external work performed when the rate of performance is constant; but the variation about the mean is considerable. These are merely illustrations. Actually, when the whole of the available observations (163) was statistically analysed, it appeared that when one attempted to predict the amount of work performed from a knowledge of the amount of oxygen consumed, the amount of carbonic acid exhaled, and the speed of performance of the work, the prediction was subject to a mean error of the order of 11 per cent. This is a peculiarly favourable case, viz. a set of observations upon one trained individual performing a simple piece of mechanical work. The

next Table derived from observations on six subjects shows a variability of higher order, 14·61.

These are simple cases. When one has the problem of assessing in terms of necessary intake the cost of a day's work by a man earning his living as a coal miner, a motor-bus driver, or a civil servant, the problem is much more complicated. One has to

TABLE 7  
MARCHING LOAD, 25 KILOS (CATHCART AND ORR)

Subject	Calories per Square Metre per Hour	Subject	Calories per Square Metre per Hour
<i>In the post-absorptive state—</i>		<i>After meals—</i>	
A	227·0	A	223·3
	205·4		213·1
B	179·0	B	185·4
			182·8
C	236·6	C	185·0
	313·7		249·6
E	195·2	C	246·0
			259·3
F	285·0	H	214·7
	264·5		248·3
	260·9		221·1
			221·1
			217·6
			220·0

Mean = 228·43 cals. Standard Deviation = 33·38.  
Coefficient of Variation = 14·61.

remember not only that the mere mechanical operations are very complicated, but that the conditions under which the work is done may make all the difference. The next Table (p. 103) illustrates the immense importance of one environmental factor.

Indeed, if we come down to bed-rock and consider the variability of the overhead cost of bare maintenance, we find it still of the order of 10 per cent. Benedict and Harris published a careful biometric study of the basal metabolism of a number of healthy adults, i.e. of the maintenance cost, when no extrinsic demands for energy are made. If no attention was paid to differences of weight, stature, or age, the variation was of the order

of 12 per cent of the average. When the standard of reference was the unit of body surface, deduced from height and weight by an empirical formula, the percentage variability was about 8 per cent. When resort was had to the method of multiple correlation, age, body weight, and height being taken as the independent variables from which an estimate of energy-use should be made, variability about the average diminished to 6 per cent.

So long as we are considering the requirements of a crowd, and in epidemiology, the crowd point of view is primary, this individual variability may not seem of much importance; but when one has to do with a group, for instance inmates of a residential institution,

TABLE 8

REQUIREMENTS OF SEDENTARY WORKER UNDER DIFFERENT CONDITIONS  
E'S RESULTS. SUBJECT: A CLOTHED MAN WEIGHING 65 KILOS

*(The figures in brackets are the estimated values of purchased food)*

Temperature	Air Current 1 Metre per Second	Air Current 3.5 Metres per Second
- 1° C.	5,406 (6,007)	6,654 (7,393)
+ 5° C.	4,000 (4,444)	4,704 (5,227)
+ 10° C.	3,060 (3,400)	3,690 (4,100)
+ 15° C.	2,317 (2,574)	2,754 (3,060)

a mental hospital, a prison, or a boarding school, it cannot be neglected. If one has to estimate the total energy requirements of  $N$  adults where  $N$  is a large number, and can make available for that class  $N$  times the *average* requirement as deduced by some experimental determination, and if each member of the class has free access to this store, it is likely enough that the needs of each member will be satisfied. But when, as in prisons, *individual* rations are apportioned it is certain that supplying each with the mean requirement so determined will result in the definite under-rationing of a sensible fraction. Suppose the variability to be in fact 10 per cent of the mean, then we should expect that no less than 16 per cent of the group will have rations 10 per cent or more in defect of their needs, and more than 2 per cent will come short to the extent of 20 per cent.

The fact that (on the hypothesis of a symmetrical distribution)

the same percentages will receive too much will be no physiological satisfaction to those who go short. Hence when strict apportionment is necessary, one must either face the certainty of hardship, fix the standard ration above, a good deal above, the average requirement, or leave some article of consumption unrationed. That was the justification of the British policy in the war days of food restriction of leaving one important source of energy, breadstuffs, unrationed.

The practical conclusion of the whole matter is that from the

TABLE 9

ENERGY REQUIREMENTS OF VARIOUS GRADES OF WORK (DEDUCED FROM AMAR'S STATISTICS)

*(The figures in brackets are the estimated values of purchased food)*

Body Weight, Kilos	Sedentary Work, Calories <i>per diem</i>	Moderate Labour, 65,000 Kilogrammetres <i>per diem</i>	Severe Labour, 130,000 Kilogrammetres <i>per diem</i>
45	1,778 (1,976)	2,733 (3,037)	3,687 (4,097)
50	1,867 (2,074)	2,822 (3,136)	3,776 (4,196)
55	1,955 (2,172)	2,910 (3,233)	3,864 (4,293)
60	2,044 (2,271)	2,999 (3,332)	3,953 (4,392)
65	2,133 (2,370)	3,088 (3,431)	4,042 (4,491)
70	2,222 (2,469)	3,176 (3,530)	4,131 (4,590)
75	2,311 (2,568)	3,266 (3,629)	4,220 (4,689)

herd point of view experimental determinations of this kind should be taken to give one an idea of the *order of magnitude* of the requirements of different classes and to give no more. Owing to a desire, begotten of human laziness out of ignorance, to accept definite, dogmatic statements there is a demand for the laying down of dietetic laws in terms of, for instance, calories. No scientific man ought to supply that demand; all he can do is to indicate the order of magnitude of the quantities. This indication, although it may be based upon very precise measurements, can, when used for the guidance of social or economic groups, never be more than a rough<sup>1</sup> one. In the above Table are some such rough indications.

They were deduced from a by no means precise study of the energy needs of a number of Arabs put to that favourite exercise

of the student of human energetics, driving the wheels of a stationary bicycle. It appeared that the data—observations made by a French engineer, Amar—were satisfactorily smoothed by the equation  $H = 6.24 W + 17.78 M + 966.50$ , where  $H$  is the total energy value of the food consumed,  $W$  the thermal equivalent of the external work done,  $M$  the body mass in kilogrammes.

Actually this table gives results in close accord with the estimates we and our fathers learned as medical students. According to it a man doing moderate industrial work and weighing 70 kilos, needs to balance his energy books about 3,200 net calories a day, or a little more than 3,500 in purchased food.

Passing now to the other method of investigation, viz. the determination of what people really do eat, immense enthusiasm has been devoted to the work, and the statistics of thousands of families and of tens of thousands of individuals have been compiled. At first blush this kind of investigation seems much easier than the experimental methods. The latter were at first horribly expensive as well as difficult. One had to possess a large calorimeter, which cost a great deal of money, as well as some manual dexterity in chemical and physical measurements. Even after the introduction of the method of indirect calorimetry, although the cost of research in money and time was reduced, the demands made upon the manual dexterity of the researcher were still considerable. Accurate gas analysis is not easily done with clumsy fingers (*credite experto*). On the other hand, the expression of the energetic values and of the ingested quantities of protein, carbohydrate, and fat yielded by food issued in schools or recorded in the accounts of patient housewives is only a matter of elementary arithmetic. Anybody blessed with patience, a table of chemical analyses, and a calculating machine must surely be able to research in this field. Life is not so simple. I have had a rather considerable experience in this kind of work and know no class of field statistical investigation where the difficulties of reaching accurate results are so many. To begin with, published analytical tables may not be applicable to the food materials actually used. "Bread," "potatoes," and "meat" are not comestibles of unvarying chemical constitution. Families are not of unvarying age and sex constitution. The diet of a family in a week of one month may differ greatly from its diet three months before or after. It is *not* easy

for the most tactful of field investigators dealing with the most patient of housewives to obtain a really complete specification of the food consumed even in a single week. In spite of these difficulties, when one is dealing with persons or families neither in intensely straitened economic circumstances nor charged with the performance of very heavy muscular work, the results of statistical studies of this kind are quite reasonably accordant. When these conditions are *not* fulfilled, comparisons should be made with the greatest caution. The principal reason why such care is needed is that in order to reduce families which differ in sex and age constitution to a common basis of comparison each member of the family is expressed as a fraction of a standard "man," and the dietetic mean is reached by dividing the total intake by the sum of these fractions. This involves two difficulties. The first is that the energy requirements of growing children even within the limits of health vary greatly; it is now generally agreed that the system of coefficients mostly used a generation ago and due to Atwater was incorrect, that, on the whole, the requirements of non-adults were underestimated. The second is that the standard "man" who has been tacitly taken as the unit of the system may not fairly represent the actual "man" of the family studied. Let us take an arithmetical example. Suppose the energy needs of a man doing light work were really 3,000 calories, and that the fractional needs of children under six were 0.4 of such a "man," of children from six to ten 0.5 of a "man," and of an adult woman 0.8 of a "man." Then the balance sheet of a family consisting of father and mother, three children under six, and one child of eight should work out:

<i>Calories</i>					
Three small children .. .. .	..	..	..	..	3,600
School-child .. .. .	..	..	..	..	1,500
Mother .. .. .	..	..	..	..	2,400
Father .. .. .	..	..	..	..	3,000
					<hr/>
					10,500
					<hr/>

The "man" value is  $3 \times 0.4 + 0.5 + 0.8 + 1.0 = 3.5$ . Dividing 10,500 by 3.5 we have the correct value of 3,000. Also, of course, if we subtract from the total the father's 3,000 calories and divide the remainder, 7,500, by 2.5 we shall again reach

3,000 calories. But suppose the father of this family were earning his bread by heavy muscular work, and in order to do his job must transform 4,000 calories, then the amount available for the rest of the family is not 7,500 calories but 6,500 calories, and their actual per "man" ration not 3,000 but 2,600 calories, a shortage of more than 13 per cent. In practice we do not often know the details of internal distribution within the family; we can make no allowance for this, so that all families having the same "man" composition and receiving the same total intake of calories will appear in our standardized statistics identical. This limitation of the applicability of the method, first, I think, clearly stated no longer ago than 1921 by Corlette, is an important one, and if the diets studied relate to a grossly heterogeneous sample of families—heterogeneous, I mean, in respect of the physical demands made on the males—might well lead to gross errors of interpretation. In everyday practice the difficulty is not so formidable as it sounds. Whatever may be the evils of our civilization, this at least may be claimed for it, that, partly by the introduction of labour-saving machines, partly by regulation of hours of labour, very gross contrasts of physical demands on energy use are growing fewer. Where this is not true, as in the life of soldiers on active service, the method of direct experiments, adequately controlled statistically, must, and in fact does, replace any method of indirect estimation. Returning to the family budget method, the numerous observations of our own time—I would particularly direct attention to the Medical Research Council's Special Report No. 101, and to Professor E. P. Cathcart and his colleagues' recent study, Report No. 151—suggest that the easily remembered prescription of our student days, 3,500 calories, given by (roughly) 100 grammes of protein, 100 grammes of fat, and 500 grammes of carbohydrate, is an overestimate of the requirements of the standard "man." As a general statistical average we might take 3,000 as nearer the mark.

Cathcart and his colleagues investigated the diets of 154 families and reached an average "man" value of 3,119 calories. In their group of manual workers the average was 3,095 calories, and the average weekly expenditure on food per "man," 10s. 9d. The average weekly income was £3 12s. 1½d. An interesting point in this thorough study was the enormous range of variation within

the same class. Take as an illustration the results for seven cleeck makers (the study was made in St. Andrews); the mean energy value is 3,281, the range from 2,386 to 4,348. The expenditure varied from 8s. to 16s. 0½d. This study, indeed, dots the i's and crosses the t's of the warning just given as to the danger of employing statistical averages for individual prescriptions. Suppose we were set this problem: A population of thirty million "men," industrially constituted as is the present population of England and Wales, has to be fed; what is the daily quantum of energy that ought to be available in order to feed this population? Then, I think, three thousand times thirty million calories would be a fair answer, subject to the proviso that this energy is *not* distributed in thirty million separate doses, but can be drawn on as individual needs demand. When, and only when, we have such a problem to solve (we did have a similar problem to solve in wartime) is this solution of much practical value. Far more often the problem is of the following kind. One has to consider the situation of persons who, unable to earn a living through no fault of their own, must be maintained from public funds and maintained in their own homes; how are the requirements of these families to be satisfied? In the solution of such a practical problem mere statistical averages are of little value. There is no statistical short cut to truth, no way of conscientiously evading the duty of direct personal investigation of the physiological circumstances of the families for which the State or the municipality is responsible.

Let us return for a moment to the illustration I gave above of seven families the breadwinners of which were all engaged in the same task. Suppose it were necessary to ration these families. We cannot say whether the maximum of 4,348 calories was mere *luxus* consumption of nearly two thousand above the minimum, because, even if all did exactly the same amount of manual work, still the efficiency of the several living machines may not have been the same. Efficiency is an ambiguous word as used in everyday life. We do not use it often in the strict schoolbook sense of the proportion of physical energy supplied to a machine, which reappears as mechanical work done. In the special case of a biological machine, if we express the relation between the external work done and the energy transformed by the body (both, of

course, expressed in the same unit, viz. the unit of heat), then if the relation were a simple linear one, i.e. if for every unit increase of work performed there were  $n$  unit increases of energy transformed by the body, a reasonably good measure of efficiency would be the ratio 1 to  $n$ . Further, this  $n$  would be constant for an individual working at a given rate, but would differ from individual to individual. Everybody knows the difference—objectively illustrated by sweating—in this respect between a trained and an untrained manual worker. Such differences, although less striking, no doubt occur within the class of trained workers. Plainly we *cannot* determine the efficiencies of even seven, not to speak of seven hundred, workers. We strike an average; let it be the arithmetic average, viz. 3,281, it is *only* an average.

Since, by hypothesis, we cannot determine the causes of the variations about the average so far as these are due to intrinsic biological factors by direct study, perhaps we can proceed by exclusion, viz. by discovering whether much of the variation is due to differences in choice of food materials, cooking, etc. This will prove almost as difficult a task as that of measuring the efficiencies of the various biological machines—not quite so difficult, for the former is impossible, while some light on the latter can be thrown by a study of family budgets. Still professional people do not all keep very detailed accounts, and it is a little unreasonable to expect those less accustomed to do sums to keep exact records. Now one begins to see the real difficulty of the administrator. If he were to fix a money equivalent of the average ration, he would be accused of underfeeding some of the families; if he takes the upper limit, then, no doubt all the families will have enough, but he will be accused of robbing the taxpayer. Like most people, I can suggest a way out. But, again like that of most people, my knowledge of the practical art of local administration is so small that I shall refrain from airing my suggestions. Perhaps Burke was right when he said—curiously enough the remark occurs in a paper on food scarcity—"Let us be saved from too much wisdom of our own, and we shall do tolerably well."

This, however, brings us to a turning-point. *Does* this arithmetical-physical way of examining the problem tell us all we need to know?

In a passage which, of course, all readers have by heart, Lucretius pictured the high gods as indifferent to the struggles of man. Perhaps one might suppose them to be faintly amused, if from the Olympian heights they look down upon us and note how disconcerted we are when the answers to the questions we put to their representative "nature" are quite different from what we expected. I suppose the man who first exposed an animal to a high pressure of life-giving and life-sustaining oxygen, and saw it go into convulsions and die, had a shock. Perhaps the great biochemist who a quarter of a century ago showed that animals supplied with all the necessary energy and building stones in the form of chemically pure protein, fat and carbohydrate, and the appropriate inorganic material—everything Victorian scientific hearts could desire—did not thrive may have passed through a moment of painful perplexity. It followed that the slogan, Science is Measurement, interpreted to mean measuring calories and weighing out proximate principles, was not sufficient; what *was* safe after this?

Since 1906 writings on the qualitative aspects of nutrition, especially those dealing with the factors of a diet which contribute nothing to its energetic equivalent, have increased so much in number and bulk that only specialists can read them. In the newspaper offices and the streets vitamins have more prestige than even calories had. It is now part of the common knowledge of educated men that sickness, even mortal sickness, can be and often has been produced by the consumption of diets which assessed by the other criteria I have discussed were quite adequate. Several symptom-complexes are known of which a qualitative food deficiency, if not the unique determinant, is at least the most important contributory cause. Beri-beri, scurvy, and pellagra will occur to the reader at once. The detailed discussion of such illnesses would be out of place here, but it will not be out of place to warn the reader against exaggeration and to illustrate the rule that the more dramatic examples of disease due to improper diet usually involve the co-operation of several factors. As an illustration which is not too hackneyed to give I take the century-old story of the Millbank Penitentiary.

The Millbank Penitentiary was a convict prison on Benthamite principles opened in 1816, and containing at the date of the

events I am about to describe some five hundred and fifty male and three hundred female prisoners all serving long sentences and employed either on moderate industrial or on hard labour. Down to July 1822 the diet was as follows: Each male aged over sixteen received  $1\frac{1}{2}$  lb. of bread and 1 lb. of boiled potatoes daily. Four days a week 6 oz. of coarse beef (cooked weight, without bone) were served; on the other days the males received a quart of broth derived from the cooking of the meat and thickened with Scotch barley, rice, potatoes, or peas, as well as cabbages, turnips, and other cheap vegetables. For breakfast and supper 1 pint of hot gruel or porridge was supplied (i.e. a pint at each meal). Women received only a pound of bread, but otherwise the same ration. Sometime before July 1822 the medical officer came to the conclusion that the prisoners ate too much, and, with the approbation of an eminent "authority" of those days, Sir James McGrigor, the following changes were made in July. No potatoes were supplied at all and no solid meat. Instead, the males received twice daily one pint of soup made from stewing an ox head in the proportion of one ox head to every hundred male prisoners, and thickening the soup with vegetables, peas, and barley. To anticipate a little, I may say that the food economists had reduced the energy value of the diet by rather more than 25 per cent, while neither before nor after the reform was any appreciable amount of uncooked vegetable food or milk supplied. Nobody seems to have seen anything amiss for some months. In the autumn, however, "the general health of the prisoners began visibly to decline. They became pale and languid and thin and feeble. Those employed in tasks requiring much bodily exertion were unequal to the same quantity of work as formerly. Those at the mill could grind less corn; those at the pump could raise less water. From time to time some of the laundry women fainted under their work; and the business of the laundry could only be carried on by continually changing the hands engaged in it."\*

The autumn passed, however, into an unusually cold winter before the epidemiological consequences of the food reform became too manifest to be disregarded. By the middle of February 1823 there was an alarming amount of illness, described by Peter

\* Latham, *An Account of the Disease lately prevalent at the General Penitentiary*, London, 1825, p. 4.

Mere Latham, one of the best clinicians of his time. The ordinary signs of scurvy were present in more than half the prisoners, and an epidemic of "dysentery" broke out which persisted after the scurvy had disappeared—probably in response to the action of the physicians called in in February (Latham and Roget), who at once ordered the substitution of 4 oz. fresh meat, 8 oz. rice, and three oranges for the soup ration, and reported that by the third week of March few symptoms of scurvy were observed. After the change of diet the incidence of dysentery was also diminished, but only temporarily; before the end of April there was a serious recrudescence. Ultimately all the surviving prisoners were removed to other gaols, but among them, particularly among the women, relapses were so serious that "the only measure which remained was to set at liberty all the female prisoners, without exception, for the sake of preserving their lives."\* During the period of Latham's attendance thirty persons died; as late as May 15, 1823, two hundred and twenty-five were suffering from diarrhoea.

Latham makes the illuminating remark that of twenty-four persons employed in the kitchens all but three were free from disease, and these three had been promoted to the kitchen staff within four days of the onset of symptoms.

This horrible business was reviewed by a Select Committee of the House of Commons, whose report contains much curious information. *Inter alia* it records that a coroner's jury which also heard some of the evidence reached this conclusion: "That the said Charles Thompson, being a prisoner in the said General Penitentiary, on June 26, 1823, then departed this life from the effects of solitary confinement and the want of the common necessities of life during his residence in the said prison, since June 29th last." The verdicts of coroner's juries are not always so sensible. This verdict includes an item which I have not yet specifically noticed: the effects of solitary confinement. The cells where the half-starved wretches spent much of their time were, it appears, so badly warmed that a temperature of 46° F. was often unobtainable. But which of the "common necessities" were deficient? All of them. Anti-scorbutic vitamin was not very abundant in the original diet; it was almost absent from the

\* Op. cit., p. 193.

revised diet. Celery, carrots, parsnips, and turnips (in the proportion of a pound for five persons) were in the soup, but in all probability were subjected to the temperature of boiling water for some time.

TABLE 10

MILLBANK PENITENTIARY, MALE PRISONERS, ONE DAY

	Pounds	Grammes			Calories
		Protein	Fat	Carbo- hydrates	
No. 1 DIET:					
Bread .. .. .	1·5	54·44	8·10	357·15	1,763
Meat .. .. .	0·2143	20·12	12·34	—	197
Potatoes .. .. .	1·0	7·94	0·46	95·26	427
Fresh vegetables .. .. .	0·2	1·07	0·24	3·71	22
Barley, 1½ gills .. .. .	—	10·83	1·41	99·26	464
Gruel .. .. .	4·0	21·76	7·20	114·32	625
Daily total .. .. .	—	116·16	29·75	669·70	3,498
No. 2 DIET:					
Bread .. .. .	1·5	54·44	8·10	357·15	1,763
Meat .. .. .	0·09	8·45	5·18	—	83
Fresh vegetables .. .. .	0·2	1·07	0·24	3·71	22
Barley, 1½ gills .. .. .	—	10·83	1·41	99·26	464
Gruel .. .. .	2·0	10·88	3·60	57·16	312
Daily total .. .. .	—	85·67	18·53	517·28	2,644
No. 1 Diet .. .. .	—	116·16	29·75	669·70	3,498
Additional meat as calculated by Dr. Hutchison .. .. .	0·1317	12·36	7·59	—	121
Total .. .. .	—	128·52	37·34	669·70	3,619

The energy yields and distribution of proximate principles are shown in Tables 10 and 11.\*

We have here a typical example of complex causation. Knowledge available before the day of vitamins would have been

\* For details of the arithmetical reduction, see Greenwood and Thompson, *Proc. Roy. Soc. of Med.*, 1918, Vol. XI (Sec. of Epidem.), pp. 61-84.

sufficient to condemn the ration, but what we have learned in the last quarter of a century enables us to understand the course

TABLE 11

MILLBANK PENITENTIARY, FEMALE PRISONERS, ONE DAY

	Pounds	Grammes			Calories
		Protein	Fat	Carbo- hydrates	
<b>No. 1 DIET:</b>					
Bread .. .. .	1·0	36·29	5·40	238·10	1,176
Meat .. .. .	0·2143	20·12	12·34	—	197
Potatoes .. .. .	1·0	7·94	0·46	95·26	427
Fresh vegetables .. .. .	0·1	0·54	0·12	1·86	11
Barley, $\frac{1}{2}$ gill .. .. .	—	5·42	0·71	49·63	232
Gruel .. .. .	4·0	21·76	7·20	114·32	625
Daily total .. .. .	—	92·07	26·23	499·17	2,668
Man value .. .. .	—	115·09	32·79	623·96	3,335
<b>No. 2 DIET:</b>					
Bread .. .. .	1·125	40·83	6·08	267·86	1,322
Meat .. .. .	0·075	7·04	4·32	—	69
Fresh vegetables .. .. .	0·15	0·80	0·18	2·78	17
Barley, $1\frac{1}{2}$ gills .. .. .	—	8·09	1·05	74·11	347
Gruel .. .. .	1·5	8·16	2·70	42·87	234
Daily total .. .. .	—	64·92	14·33	387·62	1,989
Man value .. .. .	—	81·15	17·91	484·53	2,486
<b>No. 1 Diet .. .. .</b>					
Additional meat as calculated by Dr. Hutchison .. .. .	— 0·0827	92·07 7·76	26·23 4·76	499·17 —	2,668 76
Total .. .. .	—	99·83	30·99	499·17	2,744
Man value .. .. .	—	124·79	38·74	623·96	3,430

of events more clearly. It is almost certain that even if the diet had been adequate from the point of view of energy its lack of accessory food substances would have eventually led to trouble. It is equally probable that an addition of sufficient vitamin-

containing substances, but maintenance of the low energy yield, would only have changed the clinical form of the reaction. Both errors in combination led to the particular disaster.

Some people, a little irritated by popular exploitations of *The Newer Knowledge of Nutrition*, and alarmed by the relentless march of vitamins which are now moving towards the middle of the alphabet having left the first letters far behind, have suggested that in practice, if one pays attention to our old friends the calories and is not too high-browed in one's attitude towards the likes and dislikes of human beings in the matter of food, it may not be really necessary to fuss about vitamins. There is some truth in this. Any sensible epidemiologist would agree with McCollum and Simmonds' remark that "the history of beri-beri serves as an example of the inability of pathologists or epidemiologists to solve the problem of the etiology of such a disease," and also agree that "it illustrates the value of fundamental chemical research directed towards determining the chemical items which can serve as the simplest adequate diet for man or animal."\* But such agreement does not commit one to the conclusion that even beri-beri is a *merely* biochemical problem. If civilized men had free access to unsophisticated food stuffs, the biochemical, like the energetic study of diets, would not be of much practical importance to the epidemiologist. But they have no such choice. Millions of men live thousands of miles from the source of production of the bulk of their food. Nearly everything they eat is sophisticated—partly, perhaps mainly, because without such sophistication it could not be brought to them at all; partly for the profit of the vendor. There is proof that in some very important respects, for instance the condition of the teeth, "savages" consuming diets which "civilized" people probably would not like and certainly could not get are better off than we are. There is a fair presumption—short of absolute proof, because hardly enough attention seems to have been given to the factor of racial selection, still a fair presumption—that the dietetic habits of our time are responsible for this. That is the reason why able men who are not fanatics emphasize the qualitative factor of diets. It is much easier to secure a ration which is adequate from the

\* McCollum and Simmonds, *The Newer Knowledge of Nutrition*, fourth edition, 1929, p. 213.

quantitative point of view than one which is, in the fullest sense of the term, well-balanced. Having regard to the limited range of choice open to the civilized family of limited means, natural taste is not an adequate guide. What we shall eat and drink is determined in the first place of course by plain necessity; if oysters were essential to human life, most of the inhabitants of these islands would never have come into existence; if fresh home-grown butcher's meat were an essential of life, our population would be extremely small. That is all obvious enough. But secondary factors of very great importance operate—fashion and education, for instance. A century ago many people who had no natural urge to do so killed themselves by over-eating and overdrinking, just as many people then (and now) bored themselves by telling stories which did not amuse them, or anybody else, because these were the habits of the leaders of the herd. These influences are still very powerful, indeed more powerful than ever. After all, a century ago very few people could *afford* to kill themselves with port wine as Pitt and Fox did. But now millions of people can be psychologically influenced against their own interests and in the interests of big business to believe that this or that dietetic habit is healthy. If we are to alter this we must proceed very cautiously. The warning of Lavoisier which I quoted at the beginning of this chapter has lost none of its force. True we are in no risk of being guillotined if we disregard it, but we *are* in eminent peril of being held up to ridicule as impracticable faddists. Medical officers of health should not be too eager to lead a food reform campaign. The battle is a harder one, the foe much stronger, than one may imagine.

#### RECOMMENDATIONS FOR FURTHER STUDY

*The Science of Nutrition*, by Lusk, and *The Newer Knowledge of Nutrition*, by McCollum and Simmonds, are the standard textbooks dealing broadly—of course there is a certain amount of overlap—with the quantitative and qualitative aspects of the subject. A paper by Greenwood and Newbold which appeared in the *Journal of Hygiene* (Vol. XXI, 1923, p. 440) and those cited in it might be read with advantage.

*Vitamins: A Survey of Present Knowledge* (Medical Research Council, Special Report Series, No. 167) is a complete account of this field.

## VIII

### PROCATARCTIC FACTORS—OCCUPATION

IN the last chapter I discussed, superficially and incompletely, the epidemiological aspects of diet. I will now call attention to some of the correlates of occupation which are, or seem to be, influential upon the well-being of the crowd. But the treatment is still more superficial because the subject is even more complex. Here, even more completely than elsewhere, one is deprived of the aid of clear-cut distinctions. When we contrast the sanitary experience of crowds\* whose livelihoods depend upon different pursuits we are hardly ever comparing crowds which differ only in occupation, and the sanitary experience which we make our dependent variable. Often there is a difference of economic status and all that such a difference implies; often there is a meteorological difference and what that implies; last, but not least, there is a difference in physical and mental selection.

Let us begin with the broadest kind of contrast, that between a crowd industrially employed in the current sense of the word—that is, one most of whose males and a large proportion of whose females work in factories—with a crowd most of whose males and some of whose females work, if not in the country, at least not in the large factories of a modern industrial town. Such a contrast is afforded by the different vital statistical experiences of England and Wales and Sweden. Comparison shows that although, down to a recent period, Sweden had a considerable advantage over us in respect of mortality in the first years of life, this was soon lost, and from school age onwards the English rates of mortality were much lower than those of Sweden until the prime of life was reached. In the early thirties the rates approximate and thereafter the Swedes have an increasing advantage.

The Table on the next page illustrates the point.

\* In scientific slang one speaks of *herds*, but there seems no good authority for using this word, except contemptuously, of a group of human beings. Perhaps *crowd* might be tolerable.

TABLE 12

1,000 × PROBABILITY OF DYING WITHIN A YEAR AT EACH AGE FROM 10 TO 54

Age	Males			Females		
	England	Sweden	Percentage Ratio	England	Sweden	Percentage Ratio
10	1·8175	3·22	56·4	1·9867	3·25	61·1
11	1·8293	2·96	61·8	1·9809	3·16	62·7
12	1·9507	2·80	69·7	2·0735	3·20	64·8
13	2·1413	2·76	77·6	2·2238	3·56	62·5
14	2·3690	2·85	83·1	2·3997	3·82	62·8
15	2·6107	3·22	81·1	2·5779	4·19	61·5
16	2·8517	3·88	73·5	2·7437	4·61	59·5
17	3·0860	4·52	68·3	2·8912	4·84	59·7
18	3·3161	5·33	62·2	3·0234	5·00	60·5
19	3·5516	5·94	59·8	3·1419	5·05	62·2
20	3·7825	6·41	59·0	3·2538	5·26	61·9
21	3·9987	6·53	61·2	3·3666	5·53	60·9
22	4·1899	6·46	64·9	3·4880	5·68	61·6
23	4·3353	6·49	66·6	3·6113	5·61	64·4
24	4·4414	6·38	69·2	3·7315	5·70	65·5
25	4·5393	6·28	72·3	3·8586	5·96	64·7
26	4·6598	6·28	74·2	4·0022	6·06	66·0
27	4·8342	6·14	78·7	4·1720	5·96	70·0
28	5·0720	6·14	82·6	4·3729	5·95	73·5
29	5·3528	6·14	87·2	4·5986	6·01	76·5
30	5·6629	6·04	93·8	4·8422	6·12	79·1
31	5·9885	6·06	98·8	5·0969	6·01	84·8
32	6·3158	6·05	104·4	5·3558	6·01	89·1
33	6·6416	6·00	110·7	5·6193	6·18	90·9
34	6·9753	6·07	114·9	5·8921	6·36	92·6
35	7·3218	6·37	114·9	6·1736	6·50	95·0
36	7·6859	6·39	120·3	6·4637	6·52	99·1
37	8·0725	6·54	123·4	6·7616	6·73	100·5
38	8·4711	6·74	125·7	7·0587	6·86	102·9
39	8·8787	7·15	124·2	7·3552	6·87	107·1
40	9·3114	7·87	123·0	7·6646	7·00	109·5
41	9·7863	7·79	125·6	8·0004	7·15	111·9
42	10·3201	8·03	128·5	8·3763	7·22	116·0
43	10·9101	8·30	131·4	8·7879	7·27	120·9
44	11·5461	8·54	138·2	9·2263	7·50	123·0
45	12·2344	9·25	132·3	9·6994	7·68	126·3
46	12·9814	9·42	137·8	10·2153	7·73	132·2
47	13·7940	10·01	137·8	10·7820	8·44	127·7
48	14·6620	9·86	148·7	11·3761	8·40	141·4
49	15·5827	10·92	142·7	11·9929	8·95	134·0
50	16·5749	11·24	147·5	12·6694	9·11	139·1
51	17·6580	12·13	145·6	13·4440	9·56	140·6
52	18·8523	12·75	147·9	14·3556	9·83	146·0
53	20·1569	13·46	149·8	15·4318	10·54	146·4
54	21·5630	14·45	149·2	16·6515	11·46	145·3

At the age of ten the English males died at little more than half the rate of the Swedish males; at the age of fifty-four they died almost half as fast again as the Swedish males. That is to say, in industrialized England and Wales the younger members of the crowd were better off and the older members worse off than in Sweden.

Within the same country, the same kind of contrast between industrialized and semi-rural populations is found. Seventy years ago, in 1861-5, the rates of mortality per 1,000 males aged 15-20 in the Registration County of Lancashire and the south-western group of Registration Counties were 7·6 and 5·5; in 1906-10 they were 3·4 and 2·8. The two ratios are 1·38 to 1 and 1·26 to 1. In the age group 55-65 the rates were 44·2 and 27·1 per 1,000 living in 1861-5, 41·3 and 20·1 in 1906-10, ratios of 1·63 to 1 and 2·05 to 1. The highly industrialized area compares unfavourably, increasingly unfavourably, with the less industrialized in later life; its relative disadvantage in early adult life is decreasing.

This can hardly be due to the harsher climate of the north-west. Table 13 leads to the following inferences:

TABLE 13

RATES OF MORTALITY FROM CERTAIN CAUSES, 1901-10

	Ages 45-55		Ages 55-65	
	Pneumonia	Bronchitis	Pneumonia	Bronchitis
England and Wales:				
Male .. .. .	1·53	0·73	2·49	2·66
Female .. .. .	0·75	0·62	1·44	2·29
Lancashire:				
Male .. .. .	2·45	1·43	3·85	5·09
Female .. .. .	1·20	1·33	2·27	4·60
Northants:				
Male .. .. .	0·85	0·37	1·29	1·31
Female .. .. .	0·34	0·28	0·69	1·46
Cumberland:				
Male .. .. .	1·94	0·44	2·84	1·93
Female .. .. .	0·91	0·37	1·60	1·73
Westmorland:				
Male .. .. .	0·91	0·19	1·76	0·95
Female .. .. .	0·56	0·29	0·89	0·53

If we assume that the whole of the excess mortality in Cumberland above the all-England rate is due to climatological factors and ignore the rates of sparsely peopled Westmorland altogether, it still appears that Lancastrian males die of pneumonia in the age group 44-55, 26 per cent faster than the males of Cumberland and 36 per cent faster in the next age group. They die more than three times as fast as the Cumberland males of bronchitis at 45-55,

TABLE 14

DEATH-RATES FROM ALL CAUSES PER 1,000 PERSONS, 1911-13

Ages .. ..	0-5	5-15	15-25	25-45	45-65
Bolton:					
Males .. ..	47·7	3·2	3·7	7·0	27·7
Females ..	41·8	3·0	3·1	5·6	21·0
Northampton:					
Males .. ..	36·0	2·4	4·3	5·6	18·0
Females ..	30·9	2·6	3·8	4·7	15·1
Reading:					
Males .. ..	26·8	2·2	3·0	5·5	16·8
Females ..	23·5	2·0	2·5	4·5	12·2
Warrington:					
Males .. ..	48·4	3·8	3·5	7·5	25·4
Females ..	44·1	4·0	3·0	5·9	21·0

and more than two and a half times as fast in the age group 55-65.

We may, I think, take a relatively high mortality in later adult life as a general characteristic of an industrial crowd. Why should this be? We are only paying ourselves with words if we say that the country is healthier than the town. Why is this healthiness more effective at later ages? Most people would say that countrymen have more air and sunlight, eat less sophisticated food, and worry less than townsmen. With respect to air and sunlight the nearest approach to a clean controlled experiment—and the approach is not *very* close—is given by a comparison of the vital statistics of four industrial towns: Reading, Northampton, Bolton, and Warrington (Tables 14 and 15).

Reading has an immense superiority, next comes Northampton (except in the age group 15-25\*), while Bolton and Warrington

\* This excess is largely due to tuberculosis and reflects an occupational factor; Northampton is a centre of the boot trade and tuberculosis is everywhere heavy upon shoe-makers.

have, in terms of Reading, shocking rates of mortality. The simple economic explanation dear to the heart of a platform speaker, viz. that people are much better paid in Reading than in Bolton, is quite wrong. Professor Bowley and his colleagues made a careful study of the economics of these towns. They found in Reading that 23 per cent of the working-class households had so small an all-in income that it was impossible for them to reach a

TABLE 15

MORTALITY-RATES FROM ALL CAUSES EXPRESSED IN TERMS OF READING, 1911-13

Ages .. ..	0-5	5-15	15-25	25-45	45-65
Reading:					
Male .. ..	100	100	100	100	100
Female .. ..	100	100	100	100	100
Northampton:					
Male .. ..	134	109	143	102	107
Female .. ..	131	130	152	104	124
Bolton:					
Male .. ..	178	145	123	127	165
Female .. ..	178	150	124	124	172
Warrington:					
Male .. ..	181	173	117	136	151
Female .. ..	188	200	120	131	172

physiological minimum of food and clothing.\* In Bolton only 8 per cent fell below that level. But Bolton had 78 per cent more deaths in childhood, and almost 70 per cent more deaths in later adult life, than Reading.

Evidently there is some other factor, either in the selection of the members of the crowds or in their environment. An obvious one is the difference between the smoke-laden atmosphere of industrial Lancashire and the amenities of Berkshire. Perhaps that is good enough evidence that air and sun are of importance. And diet? I have no relevant data, but I would remind the reader of an old joke in *Punch*, that of the seaside landlady who, enumerating the advantages of the town, mentions that as it is only an hour from London one can have fresh fish for breakfast.

\* Whether the standard was not pitched too high is an irrelevant question. See Bowley, A. L., and Burnett-Hurst, A. R., *Livelihood and Poverty*, London, 5, with Supplementary Chapter (on Bolton), London, 1920.

There is a good deal of evidence, especially from Ireland, that one goes shortest of bacon, milk, and butter in the areas of maximum production if those areas are blessed with a properly organized system of transport to industrial areas. The country fare of poetic descriptions is not by any means always to be found easily and cheaply in the country.

Lastly, worry and the strain of life: what of these? There is an enormous literature, from the Romans onwards, expounding the advantages of country life. A majority of the best expounders of this philosophy happen to have been men about town; of the three Romans who especially distinguished themselves in this *genre*, Vergil, Horace, and Martial, the last two were men about town for a good deal of their time. However, as one of them said, *Video meliora proboque, deteriora sequor*, and the preacher who reckons not his own rede may preach very sound doctrine.

I do not myself know of any way in which the "strain" and "pace" of life in towns, or, alternatively, of modern life (a reader will note that I have used each of the *clichés*), can be measured, one difficulty being, no doubt, that nobody has yet defined any of these things in an unambiguous way.

Because a man is not always weeping on one's shoulder it does not follow that he is unemotional; because peasants are not exhibitionists it does not follow that their lives are free from "strain." As an epidemiologist I am hardly better off than the moralists; like them I can only guess. My *guess* is that units of the industrial crowd falter and break down in the later adult ages more easily than members of the non-industrial crowd because of the discontinuity of their life. *Young* members of the town crowd have a much fuller and more interesting life than the young countrymen; it is hardly more exciting to learn the elements of agriculture than the duties of a factory or office subordinate, and town lads can go to the pictures, football matches, and even own motor-bikes; but the time comes when motor-bikes and the pictures have lost their attraction. An ageing townsman of the insured class is losing the alleviations of his boring occupation, but the boredom remains. A peasant knows less about agriculture than his master, but his knowledge is of the same kind. He does see life whole, and when he is past work can still be interested in the work. The factory hand or the commercial subordinate

in big business may be narrow specialists, while their education seldom provides them with the means to cultivate gardens, either literal or metaphorical gardens, an advantage which the old-fashioned liberal education did give a minority of the professional classes.

The late Dr. Wanklyn, in one of the most moving papers I have ever read, has described the effect of environmental conditions which (*of course*) have long passed away. He spoke of the "general want of colour and relief in the surroundings." "The dinginess and monotony of such houses and streets," he wrote, "contribute materially to depressing the health of those who live in them. Let anyone who is fairly well off and robust and well-educated attempt housekeeping in these conditions; it is a great strain and a wearing struggle to be clean and decent. But for those who are ill-paid, ill-fed, and fagged out, the obstacles to decent living are too great and the struggle is too unequal. . . . The problem for the breadwinner is the same as for any other business man. If he is not paying his way he must increase his income or reduce his expenses, or do both. Persons so placed may make some effort, and wear out body and soul in the process, or they may just sit down, as it were, and give it up; the task is too hopeless, too impossible for any human being. They lose heart, they lose hope, they lose self-respect. It is an oft-told tale, but none the less true."\* That would be (again, *of course*) an exaggerated picture of the environment of the ageing small townsman, but the monotony and the sense of futility, the unspoken, even unthought, thought, that life really is "a tale told by an idiot full of sound and fury signifying nothing" which colours the emotions of most educated men every time they read a London newspaper, is not perhaps confined to highbrows; it may even contribute to our general rates of mortality. Fortunately the psychological factors of morbidity at least are now a serious object of study, so that one of my successors may be able to *measure* what I can only guess the existence of.

All this is, however, guesswork. A more precise idea of the general procatarctic factors so far as they may be measured by mortality-rates is afforded by the Registrar-General's decennial analysis of mortality in occupations. The last published report,

\* *Proc. Roy. Soc. Med.*, 1913-14, Vol. VII (Sect. of Epidem.), pp. 6-7.

which relates to the years 1921-3, is a document the reader should study carefully. Not only is the classification more satisfactorily occupational than it had been before, but a valuable comparison of the changes in mortality, both from all causes and from particular important causes as one descends the economic scale, is provided. For the purpose of this comparison the occupational groups were allotted to five classes thus defined:

Class I	..	..	..	..	..	Upper and Middle
Class II	..	..	..	..	..	Intermediate
Class III	..	..	..	..	..	Skilled Workers
Class IV	..	..	..	..	..	Intermediate (includes Agricultural Labour)
Class V	..	..	..	..	..	Unskilled Workers

There must, of course, be some overlapping, and there might be doubts as to the proper assignment of this or that occupation; still, in a general way there can be no doubt that in passing from Class I to Class V we are really passing from the prosperous to the unprosperous members of the community. Of the various methods of assessing relative mortality discussed and used in the official report I take the comparison of deaths registered between the ages of twenty and sixty-five with the deaths which would have been registered had the rates of mortality in age groups of the class or occupation (*vide infra*) been identical with those for all occupied and retired civilian males. In the third column of Table 16 we have the observed deaths as percentages of the expected deaths. It will be seen that the least favoured class experiences a mortality half as large again as that of the most favoured.

This method of global comparison is open to the theoretical objection that some particular occupation, if it is both very populous and economically homogeneous, might colour the statistical average of the class containing it too strongly, and to the practical objection that it gives no indication of the intra-class range of variation.

On general statistical grounds (such as the fact that errors in "weights," unless highly correlated with errors in "variables," are of much less importance than errors in "variables") the former objection was not likely to be of much importance, but the second point is of interest. I have accordingly had the following analysis made. The occupations included in each class were tabulated,

those so small that less than fifty deaths were registered in each during the triennium of observation were excluded; for each of the remainder the ratio of observed to expected deaths was taken as the variate. For each class the mean, standard deviation, and coefficient of variation of the included variates were computed. The results are shown in the fifth, sixth, and seventh columns of the Table. It will be seen that this method does slightly close up the interval between highest and lowest, but that the gap remains wide. It also appears that the intra-class variation is large;

TABLE 16

SOCIAL CLASSES, 1921

*Ratio of registered to 100 calculated deaths*

Class	Number of Males aged 20-65 (Census 1921)	R.G.'s Figures (Weighted)	Unweighted Results			
			Number of Sub-groups	Mean Ratio of Registered to 100 Calculated Deaths	S.D.	C. of V.
I	225,618	82	22	93	32.91	35.42
II	1,974,884	94	56	90	28.47	31.70
III	4,218,715	95	197	100	26.34	26.29
IV	1,984,906	101	83	112	35.25	31.56
V	1,300,737	125	33	120	49.76	41.62

largest of all in the worst class. In other words, even in the professional class, in spite of the tendency to uniformity in the habits of life of members of an economic class there is much diversity, and, presumably, much remediable variation from the norm of healthy living. Of the groups comprised in the worst class, thirty-three in number, nine have mortalities less than the average of the highest social class. *En revanche*, this lowest class includes five with mortalities exceeding the standard by 50 per cent or more. In a general way, the result is encouraging, since it suggests that a levelling down of mortality is taking place (another sufficiently clear indication is, of course, the general reduction of infant mortality with which all are familiar). That does not mean there is neither ground for complaint nor field

for research. The intra-class variability is still large and it is not clear that it is *unavoidably* large.

It is partly because of the levelling down of mortality in the human population that the present tendency of research is to concentrate upon morbidity rather than mortality. The desirability of this, its essential importance from the standpoint of *preventive* medicine, is obvious enough, yet it is well to guard oneself against exaggeration. More than seventy years ago Walter Bagehot in a criticism of Charles Dickens made this comment:

"He began by describing really removable evils in a style which would induce all persons, however insensible, to remove them if they could; he has ended by describing the natural evils and inevitable pains of the present state of being, in such a manner as must tend to excite discontent and repining. The result is aggravated, because Mr. Dickens never ceases to hint that these evils are removable, though he does not say by what means. Nothing is easier than to show the evils of anything. Mr. Dickens has not infrequently spoken, and, what is worse, he has taught a great number of parrot-like imitators to speak, in what really is, if they knew it, a tone of objection to the necessary constitution of human society."

These parrot-like imitators have multiplied enormously in the last seventy years, and their parrot-like insistence upon research into this or that evil of modern life is sometimes a serious obstacle to real research, because, having no conception of the complexity of the problem of interrelated group factors and a simple faith in the doctrine that what is not recorded did not happen, they are apt to believe that some particular evil ("noise," for instance) is both easily remediable and quite new.

#### RECOMMENDATIONS FOR FURTHER STUDY

Everybody should study *The Registrar-General's Decennial Supplement, England and Wales, 1921. Part II, Occupational Mortality, Fertility, and Infant Mortality*, London, 1927. Textbooks on health and occupation are numerous. For obvious reasons I think *The Health of the Industrial Worker*, by E. L. Collis and M. Greenwood, London, 1921, a meritorious volume, and I doubt whether the march of mind since 1921 has been so rapid that what seemed to be true in 1921 is now false; still, other books have been written since.

## PROCATARCTIC FACTORS—PSYCHOLOGICAL

IN the last chapter I spoke in passing of certain *imponderabilia* which play their part in determining the health or sickness of a crowd: the psychological factors. I propose now to discuss these not in detail but with a little more precision.

If one looks up the word *ψῦχῆ* in a Greek dictionary one will find its primary meaning to be *breath*, "especially as the sign of life, *life, spirit*" (I am quoting from the abridgment of Liddell and Scott's lexicon which I used at school). Then one will read that the secondary meaning is, "*the soul of man*, as opposite to the body; in Homer, only a departed *soul, spirit, ghost*, which still retained the shape of its living owner." Further on, one will read that it also may mean "the seat of the will, desires and passions, the *soul, heart; desire, appetite*. III. *The soul, mind, reason, understanding*."

Many of these italicized words are used by all of us almost every day of our lives, as is the directly derived word *psychology*, the science or lore of the psyche, and mean to us very different things, not even the same different things to different people. Take any three of them, say *soul, heart*, and *desire*, and let the reader try on himself an association test, viz. write down the first ideas or mental pictures they call up. To me *soul* called up a picture of a small bird fluttering in a ray of light; *heart*, somebody being kind to somebody else or weeping; *desire*, the thought of sexual satisfaction. The object of this prelude is not to provide the reader with data for the psycho-analysis of the writer, but to illustrate the complexity of verbal associations which again illustrate and depend upon inherent and ineluctable complexities of the ideas these words were used to convey. From the beginning of human thought the difference between the living, breathing animal and the one from whom the *breath* of life was gone must have been as evident as to us, and it was a very small flight of fancy to suppose that the breath which had given life to what was now an inert mass survived elsewhere. "Then shall the dust return to the earth as it was: and the spirit

shall return unto God who gave it." From the beginning of what we may call logical thinking, the relation between this breath of life and the body has exercised the minds of men, and the theories that have evolved fall into three main groups. In the first place that doctrine which is explicit in the text from Ecclesiastes I quoted was rationalized by Plato, who conceived the relation between psyche and body to be that of agent and instrument; the psyche used the body as a sailor navigated a boat. On the other hand, Aristotle conceived the relation differently. For him, the living man was not a "soul" using a body but an ensouled body; psyche was manifested in the body; life in the fullest sense was the impression of the seal on the wax, or, as the scholastics (through whom the Aristotelean doctrine, greatly elaborated, became part of European culture) said, the "soul" was the form of the body. Thirdly, the pupils of Epicurus, whose teaching was made available to later ages by the great poet Lucretius, believed that "soul" and "body" were both mortal and died the same death. Upon thought down to post-Renaissance times the two former hypotheses exercised more direct influence than the third. The first is more easily reconciled with the primitive religious fancies of mankind than the second, and was expounded by one of the most perfect literary artists; consequently, in various modifications it coloured the thought of the most influential fathers of the Early Christian Church, such as the great teacher St. Augustine of Hippo. The immortality of the "soul" in terms of this hypothesis is a *relatively* simple conception; but in terms of the second hypothesis the conception of immortality is a very difficult one. Remember the Cheshire Cat in *Alice's Adventures in Wonderland*. The Cat vanished, but its grin remained. The artist tried, and of course failed, to depict a grin without a cat. He might have depicted in many ways some little "spirit" living in the body of the cat which moved the cat's features into a grin, but he could not draw a grin without the grinning features. The reality of form independent of the matter expressing it is a difficult idea, and it needed a great intellectual effort to express an idea, which at first sight seemed heretical, in such a way as to make it the kernel of orthodox Christian philosophy. This revolution was carried through mainly by St. Thomas Aquinas, whose general psychology is available in a small modern edition which can be

read through in a few hours but has taken me more than a few even *partly* to understand.\*

In the relatively early days of such discussions, in the age of Hippocrates and even in that of Galen, physicians, although they might differ in the speculative views they held on the soul-body relation, did not doubt that, as physicians, they were just as interested in the psyche as in the body. Galen, in fact, discussed the psychological elements of ill health at great length and with his habitual shrewdness. In particular he protested violently against an exaggeration of one particular *aspect* of the psyche which, first expressed in the form of Stoicism, and, after his day, in that of Christian Asceticism, persistently regarded man's *conscious* reason, i.e. one aspect of his psychological life, as paramount.

But with the decay of the Graeco-Roman world and the supremacy of the Christian Church the study of the soul-body relation became a branch of theology with which professional physicians did not meddle. When Macbeth asks the physician whether he cannot "minister to a mind diseas'd," whether he can

*"Cleanse the stuff'd bosom of that perilous stuff,  
Which weighs upon the heart?"*

the physician answers:

*"Therein the patient  
Must minister to himself."*

An orthodox answer in the Protestant England of the sixteenth century. In the eleventh century, when Macbeth lived, the physician would also have shifted the responsibility from himself, but to Holy Church, not to the patient. Had Galen been asked the question he would have accepted the responsibility for himself.

The consequence was that after the Renaissance, physicians continued for, literally, centuries to ignore the old psychologies as outside their sphere, irrelevant to their work. Sometimes they expressed this feeling demurely, as when Sir Thomas Browne writes: "Where I cannot satisfy my reason, I love to humour my fancy; I had as lief you tell me that *anima est angelus hominis*,

\* Sancti Thomae Aquinatis, *Questiones disputatae de Anima*. Edited by F. Hedde, Paris, 1912 (Librairie Victor Lecoffre).

*est Corpus DEI*, as *Entelechia*." For him the difference between Platonism or Neo-Platonism and Aristoteleanism or Scholasticism is of no practical importance. Sometimes they were materialist in the worst sense of the word, as when Sydenham "explains" hysterias in terms of disorderly motions of hypothetical "spirits." Most men despise what does not interest them or what they do not think important, and if, in the perverse way things happen in real life, the supposedly unimportant becomes extremely important they become angry. Our great-great-grandparents passed from laughing at the ludicrous Corsican upstart to cursing the French tyrant and enemy of mankind. So more recently the medical profession passed from jeering at academic psychology to violent opposition to the dynamic psychology of Freud, from half-suggesting or more than half-suggesting that bodily ailments for which no "organic" basis could be found were malingering to grudging admissions that in such disorders as the shell shock and "disorderly action of the heart" of war and telegraphist's cramp or miner's nystagmus of peace, the psyche of the psyche-body partnership was of *medical* importance.

It may be said that the medical profession has merely at long last accepted the philosophy of all sensible people. It does not need much psychological insight to realize that the presence of one or two psychological misfits in a week-end party, a cricket team, or an office may destroy the happiness and efficiency of the group. But that is not a just sneer. In the examples from day-to-day experience just cited, the trouble was recognized from the first to belong to the psychological sphere. The change in essential attitude has been a recognition that end results which belong to the corporeal sphere, symptoms and signs which fall within the experience of physicians, may really be manifestations of psychological illness.

The acceptance of this point of view has no doubt been hastened by the circumstances of the world in which we live. It is a mere commonplace to say that ages of transition, when a long-established order of society is dissolving, are characterized by individual and crowd emotional reactions.

Such mass-hysteria (to use an inaccurate but common expression) has particularly characterized epochs of social transition, either before or after a period when the struggle for bare existence

has been all-absorbing. Perhaps that is why the psychological revelations of such writers as St. Paul of Tarsus or St. Augustine of Hippo are more relevant to *our* emotional experiences than those of possibly abler writers of earlier or later times such as Plato and St. Thomas Aquinas, not so acutely conscious of living in a world of change. A whole nation going "Bolshy" or "Nazi" would not have surprised St. Paul of Tarsus or St. Augustine of Hippo as much as Plato or Mr. J. L. Garvin (no disrespect either to Mr. Garvin or Plato is intended).

A striking example of the change of attitude of which I spoke is provided by the history of opinion on telegraphist's cramp, which was the subject of a report by a Committee appointed by the Industrial Health Research Board (then the Industrial Fatigue Research Board) in 1927. This report shows that although a departmental committee which reported in 1911 accepted the conclusion that the disability was due to some disease of the central nervous system, that committee failed to discover any "organic" defect, and in describing the signs and symptoms in particular cases made free use of ill-defined terms, such as "nervous instability," "temperamental factors," "highly strung disposition," leading to the conclusion that psychological predisposing factors were of importance. By 1926 this view had become almost orthodox; a writer in a German textbook published in that year stated bluntly that "since we are dealing with a 'neurosis,' that is with a purely functional and not organic illness, anatomical changes cannot be demonstrated, and so far never have been demonstrated." This writer (Kurt Mendel) described no less than thirty-four occupational "cramps" of the upper limb.

The investigators of the Industrial Health Research Board's Committee—Culpin, Farmer, and May Smith—were able to show that *as a group* the victims of telegraphist's cramp were psychologically differentiated. It was found that while, in groups of learners and of non-cramp telegraphists, the percentages showing severe symptoms of psycho-neurotic temperament were 19.0 and 32.5, in a group of cramp subjects the percentage reached 75.6. The numbers tested in the three groups were 100, 46, and 41. It was also found that when the group of learners were subsequently reported upon by their official superiors with respect

to efficiency as telegraphists there was correlation between efficiency and lack of psycho-neurotic signs and symptoms. For instance, of the males 36.5 per cent were assessed by their superiors as very good or good telegraphists. Had those learners assigned to the worst psychological group been rejected, the percentage of efficients would have been 44.4. The data are scanty and the change is only 2.6 times the "probable error" of sampling, so that the result, standing alone, would be inconclusive. It is, however, but one of many similar findings in this and other fields. While it is certain that some persons whose psychological make-up is unfavourably assessed may not suffer from the particular occupational disability studied, there seems little doubt that the group of such persons is sure to react unfavourably.

A similar result has been reached in a field of research which has been more widely cultivated, that of industrial accidents. Ethel Osborne and H. M. Vernon showed in 1922 that the incidence of minor accidents in a projectile factory was appreciably influenced by speed of production and by the temperature of the workplace. When the temperature was 67° F. to 72° F. there was a minimum accident rate; the frequency of accidents increased as the temperature fell, so that at 52° F. accidents were 35 per cent more numerous; when the temperature rose above 72° F. there was also, in departments employing men, a rapid increase. This correlation seemed to fall within the physiological sphere, because one could easily think of simple physiological reasons why there should be an optimum working temperature. A series of researches, which began in a purely statistical study of the distribution of multiple accidents, i.e. of the relative numbers of persons exposed to risk who, in an assigned period, sustained 0, 1, 2, . . . , accidents, has established the fact that some persons have a particular tendency to suffer accidents, and that this peculiarity is correlated with psychological qualities which can be explored by clinical and experimental methods. It has been fully established that in the prevention of accidents psychological factors are quite as important as, perhaps more important than, material ones.

In Haeser's classical history of medicine one will find in the part dealing with the epidemiology of the Middle Ages a special

section devoted to *Psychische Seuchen*, Lycanthropy, the Dancing Mania, the Pilgrimages of Children. Nobody has any difficulty in regarding a village the inhabitants of which come to believe that many of their neighbours are were-wolves or vampires (a belief shared by the supposed were-wolves) as suffering from a psychological epidemic; there is equally little difficulty in classifying an epidemic characterized by an irresistible desire to dance to the point of exhaustion. When flocks of children wander hundreds or even thousands of miles away from their homes eventually to die or be sold into slavery, very few people would deny that we have to do with a "disease" of the soul. But it seems a very far cry from such melodramatic happenings to, say, the "nervous debility" or the "appendicitis" of modern medical certificates.

We think we can easily understand how, perhaps bad feeding, perhaps bodily exhaustion, any or all of the physiological errors which might lead to "hysteria," have done so. It is not so easy to think we understand how *too* carefully sheltered conditions of life might work through the "soul" upon the body and precipitate a "real" attack of appendicitis. Of course the translation of body into soul is just as unintelligible as its converse. The old way of looking at the mind-body relation made it *seem* a little easier. If we think of "man" as an ensouled body, the relation being something more intimate and subtle than that of a "soul" using a "body" as its instrument, it is perhaps not quite so hard to think of a reciprocal relation, a mutual relation, and therefore not so difficult to suppose that the psychological change may be antecedent, not consequent, in a pathological nexus. But whether this is easier to understand is a matter of temperament. To me the scholastic "jargon" of form, substance, and matter brings a certain illusion of clearness; to many readers it seems a mere darkening of counsel. In any case it is certainly not my business as an epidemiologist to expound psychology of which I know little or metaphysics of which I know even less. But it is my business to point out that while a fairly consistent description of the aetiology of such crowd-diseases as miners' nystagmus, of the differences (often enormous differences) between the incidences of sickness upon the staffs of different firms and of the genesis of industrial accidents, can be provided by means of the

hypothesis that the psychological element in the mixture of interactions expressed in bodily illness is the determinant, methods which have ignored that element have led to no consistent accounts of the facts at all. For this severely practical reason I hold that practical epidemiologists cannot afford to neglect psychology. *What* psychology they should study is not for me to say.

#### RECOMMENDATIONS FOR FURTHER STUDY

I have reason to believe that Einstein's papers are not easily understood by readers who quail before a determinant, that, in fact, it is rather difficult to establish friendly relations with tensors unless determinants will eat out of one's hand. By analogy, I am led to think that before one studies the works of modern dynamic psychologists it may be prudent to examine older and no doubt more superficial accounts. Dr. May Smith and I have tried to render some first aid here. (*British Journal of Medical Psychology*, Pts. I and II, 1934.)

*PART II*

**SPECIAL ILLUSTRATIONS**



# I

## THE TYPHOID GROUP

IN the First Part of this book I have tried to explain the general principles of epidemiology and to describe the more important methods of investigation. It is possible that this Part may interest students who are not professionally concerned with public health matters. Now it is my duty to apply these principles to particular cases of crowd-diseases amongst men. Writers on epidemiology have usually assumed that their subject-matter was confined to the illnesses which are, as the man in the street would say, typically infectious, and even with this limitation the subject-matter is so vast that the most perfunctory attempt to deal with it means writing a large volume. My definition of epidemiology covers a still wider field of events; as it appears to me, a complete treatise would deal with *every* "disease" from the point of view of the crowd. The most diligent of compilers would decline the task; all I will attempt is a selection of what seem to me representative special cases.

The whole group of illnesses, an important particular case of which is associated with infection by the *B. typhosus*, have in their crowd-aspects so many common features that they may be regarded as typical of illnesses which, if we might speak teleologically, are the punishment (usually vicarious) of bad habits of eating and drinking. Cholera has many affinities with but important differences from the group. Diphtheria, scarlet fever, and measles typify very prevalent illnesses which mainly affect children. Plague and typhus are the great exemplars of pestilence, not really on a grander scale than influenza, but suffered, or at least recorded, in more dramatic settings. Influenza is—influenza! The crux of epidemiology. The venereal diseases, cancer, and tuberculosis—each subject illustrates in its own way an aspect of crowd-experience which the epidemiologist must understand.

My reason for choosing the typhoid group as the first of the selection of special topics to be discussed is that in these days optimism is at least a pleasant vice, and I know of no other illnesses in respect of which the evidence of man's theoretical

and practical capacity to control them is so cogent. I have little love of the violent metaphors of conquering or stamping out this or that sickness, but they might be applied here with less exaggeration than in many branches of practical epidemiology.

To those who read a textbook on medicine for the first time, and note the clear-cut descriptions of the "typical" signs and symptoms of typhoid and typhus, it may seem that our ancestors were very incompetent observers and foolish people to confuse things so plainly distinct. That inference can only be drawn by those insensitive to "atmosphere." For more than a hundred years, consciously or unconsciously, the criterion of likeness or difference has been a biological one. If—as indeed might happen—we were presented with two "cases" of individual sicknesses in which the clinical features were identical but the biological *materies morbi* distinct, we should inevitably think of them as different "diseases." To our ancestors before Fracastori this biological element was unknown, and even after Fracastori unimportant; their differentiae were clinical, and when the clinical forms of a "fever" did differ they did not think it necessary to allot the types to essentially different categories. They were little, if at all, interested in the differentiae from the epidemiological, although greatly from the individual, point of view, i.e. from the point of view of individual prognosis. The beginner need not suppose that Sydenham, Morton, or Heberden was less competent than he to distinguish a "case" of typhus from a "case" of typhoid, but only that these physicians were less alive to the general hygienic implications of the separation than we are. Indeed, a century before the formal separation of typhoid from typhus, Huxham, to name only one writer, did carefully describe the clinical difference between the putrid fever, our typhus, and the slow nervous fever, our typhoid. It is not even quite just to say that our ancestors had no interest in the epidemiological side. Their biological aetiology was, no doubt, erroneous. Since, on the whole, typhoid was a less serious illness than typhus, and since—in days before the existence of communal water supplies—it probably showed itself in dramatically epidemic form less frequently than typhus, they conceived that in typhus the mixture of the elements of man was more gravely disturbed than in typhoid, that there was a definite corruption or putrescence

of a humour; so that to them (as, indeed, to many intelligent persons even as recently as the nineteenth century), although typhus could not become typhoid, typhoid might pass into typhus, yet they were quite alive to what they would have called the procatactic factors of typhus. Before the eighteenth century, physicians knew as well as we do the rôle of sordid overcrowding and underfeeding in the generation of typhus.

In a word, at the end of the eighteenth century the clinical differentiation of typhoid and typhus was already fairly complete, although difference of opinion existed whether two admittedly different clinical forms were aetiologically distinct in the aetiological sense of modern science. The medical profession in England was slow to accept the distinction, not because the English physicians were dull-witted, but because at the time the discussion arose in France there was in that country a good deal of typhoid and very little typhus; in England there was little typhoid and much typhus, so that the English could not verify the findings of their French colleagues. We were convinced by William Jenner, whose paper, read before the Royal Medical and Chirurgical Society on December 11, 1849, is worthy of attention. Although Jenner, primarily a clinician, put most stress upon individual phenomena and concerned himself with the specification of "typical cases," he also relied upon epidemiological evidence to the effect that there was a *group* difference between typhoid and typhus, as the following passage illustrates:

"In November and December 1848, forty-eight cases of typhus fever and twenty of typhoid fever were admitted into the hospital, i.e. nearly one-third of the patients were affected with typhoid fever. At the latter end of October 1848 a boy fourteen years of age went to reside with a family named Mitchell, in Adden Place, St. Pancras. The Mitchells were at that time in health. The boy left his own home because his brothers were 'down with the fever.' This lad was, early in November, admitted into the hospital suffering from typhus fever. Early also in the same month the man Mitchell, aged 29 years, with whom the boy lodged, the man's daughter, aged 7 years, and a female lodger, aged 22, were also admitted with typhus fever. The other members of Mitchell's family, expelled from Adden Place, then removed to 21 Hertford Street, at least a mile from their former residence. At this time as far as I could learn by personal inquiry there was no fever in Hertford Street, and *certainly* none in the house in which they took up their residence. On November 22nd, the two sisters of Mitchell's wife, aged respectively 14 and 22,

who had removed from Adden Place with Mrs. Mitchell and her infant, aged 4 years, were received into the hospital, both suffering from typhus fever. On December 9th the landlady of 21 Hertford Street, aged 60 years, was admitted with a very severe typhus fever; and on December 20th the son-in-law of the landlady was also admitted with the same disease. I subsequently saw Mitchell's infant, aged 4 years, at its own home; it was similarly but very slightly affected. The only member of the family that escaped was the woman Mitchell, and she had had 'spotted typhus fever,' according to her own voluntary statement, some few years before. Here was a group of persons, whose ages varied from 4 to 60 years, and whose constitutional predispositions also must have varied infinitely, for there were several of them unconnected by blood, exposed to the poison of typhus fever (introduced among them by the lad aged 14) at a time when typhus fever was only twice as prevalent as typhoid fever. What was the result? Did one-third of the eight have typhoid fever? No, no one."

Jenner cites similar instances. No doubt this is only epidemiological in a humble way—in fact, to pursue a botanical simile, it is no more than attempting to demonstrate that the "plant" breeds true—but it does, I think, transcend the purely individual aspect. Soon after this, other group characteristics were sought and between 1850 and 1870 established, or at least adopted. On the one hand it was held that although *typhus* might arise, as it were, *de novo*, the chief factor of its distribution was contagion; an epidemic of typhus arose in a group when contagion was introduced and other factors (leading to lowering of individual resistance, e.g. hunger, mental depression, overcrowding, etc.) were favourable. *Typhoid*, on the other hand, was not contagious, but due to fouling of food, water, or air either by a specific *materies morbi* or by some unknown product of decomposition. The belief in a specific *materies morbi* always passed on, mediately or immediately, from a *patient*, brilliantly maintained by William Budd, did not at first make much headway in the profession as a whole; indeed, the great clinical epidemiologist Murchison never accepted it. Budd, almost the last of the old race of epidemiologists, was one of our great men, and his book on typhoid fever is a classic. The following extract is lengthy, but since it is complete in itself and an epitome of Budd's style and methods, I do not hesitate to reproduce it.

"On October 24, 1866, my friend Dr. H. Grace, whom I had met on other business, told me that if I had half an hour to spare he would

show me a striking illustration of my views on the spread of typhoid fever.

"The temptation was too great to be resisted; so, jumping into his dog-cart, we presently pulled up in front of two labourers' cottages built in a single block, by the roadside. These cottages may be called, for convenience' sake, Nos. 1 and 2. In the form of a lean-to against the gable end of No. 2 was a privy, which served in common for the inmates of both dwellings. Through this privy there flowed, with very feeble current at that time, a small stream, named the Wayne-brook, which formed a natural drain for it. Having already performed the same office for some twenty or thirty other houses, higher up its course, this stream had acquired, as was patent to more than one sense, all the characters of a common sewer, before reaching the cottages in question. From this point, after skirting the high road for about 40 or 50 yards, it passed into a field, and crossing, now as an uncovered drain, some three or four meadows, the stream came into the open again in a large court occupied by two other labourers' cottages and some farm buildings. These two cottages may be conveniently called Nos. 3 and 4. The sanitary relations which the stream held to their inmates was an exact repetition of that which obtained in regard to Nos. 1 and 2 already described. Passing through the court uncovered, it acted as a drain to a small privy, common, as before, to both cottages. I did not measure the distance which separated these two little homesteads, but I judge it to be somewhere about a quarter of a mile, as the crow flies. The four cottages thus situated were the scene of the series of events which Dr. Grace was anxious to bring before me.

"The outbreak began in the person of the father of the family living in No. 1. There were two circumstances attaching to this man which made his case different from that of any member of his own or his neighbour's household.

"1st. He was the only one of the group whose way of living took him away to the neighbouring city: and

"2nd. He was the only one who was known to have been exposed to the infection of typhoid fever.

"Having a horse and cart, he plied a small trade with Bristol, partly as a hawker and partly as a huckster. His chief business in the city lay in the filthy back-slums of St. Philip's, where, for some time immediately before his illness, typhoid fever—as I can affirm from my own observations—was epidemic. Whether he got his fever here, it is, of course, impossible to say with absolute certainty, but that in the course of his business he must have been largely exposed to its specific infection there was no doubt. That his disease was contracted away from home was further indicated by the fact that when he was stricken all the other inmates of the two cottages were, and, indeed, continued for some time after, to be, in their usual health.

"His attack proved to be severe and protracted, and for a considerable time was attended by a profuse diarrhoea. As a matter of course, all

the discharges were thrown into the common privy. In this way, for more than a fortnight, the stream which passed through it continued to be daily and largely fed with the specific excreta from the diseased intestine of the patient.

"Some weeks passed away thus, without any fresh incident; but, in the latter end of the third, or beginning of the fourth week—which, as M. Piedvache has justly observed, is about the time when the contagion of this fever generally begins to show itself in fresh crops of the disease—a new order of events occurred.

"Several persons were simultaneously attacked with the same fever in all the four cottages. Not, be it observed, in Nos. 1 and 2 merely, whose inmates might be described as living in more or less contiguity to the already infected man, but in Nos. 3 and 4 also, nearly a quarter of a mile away.

"Within the space of a few days Dr. Grace was attending quite a cluster of cases in each of the four, and before long the majority of the persons living in them were in bed with the fever. One fact must be recorded to render the history complete. From first to last, the outbreak was confined to these four cottages, and there was no other case of typhoid fever at the time in that neighbourhood.

"These facts speak for themselves. If we look at them by the light of what has gone before—if, especially, we bear in mind the established fact that, in some way or other, this fever has the power to propagate itself, there can be no reasonable doubt that the second crop of cases was the offspring of seed cast off by the first sufferer. But if this be so, the circumstances of the outbreak in the two lower cottages, Nos. 3 and 4, show by the most striking evidence what was the particular form under which this seed was liberated. The significance of these circumstances will be appreciated at once when it is added that those who were attacked in this particular outbreak had not only held no intercourse of any kind with the inmates of Nos. 1 and 2, but had not the remotest suspicion of the origin of the deadly pest which had appeared thus silently in their midst.

*"The little stream laden with the fever-poison cast off by the intestinal disease of the man who had been stricken with the same fever some weeks before, was the only bond between them.*

"We have already learnt to see in this disease of the intestine the specific eruption of a contagious fever; we here see, as in smallpox, and other contagious fevers, the poison shed by this eruption producing fresh fruit.

"But if the remarkable history here related shows with the utmost clearness that sewage when charged with the specific excreta of typhoid fever is all-potent in the propagation of that disease, it appears to me to show with equal clearness that sewage not so charged has no power of the kind.

"While Dr. Grace was seeing his patients in Nos. 1 and 2 and I was standing outside, a gentleman on horse-back drew up, and addressed

me in these words: 'Ah, I see what you are upon. The only wonder is, that all these poor people have not died of fever long ago. For, any time these last six years, but in summer especially, to anyone coming down this lane, the stink has been enough to knock a man down.'

"But although—so to speak—strong enough to knock a man down, it had failed all these long years to cause a single case of fever.

"How, if sewage emanations be as potent to cause typhoid fever as many teach, can this possibly be explained?

"This failure, to recur to an argument used once before, could not have been because the seasons had not been favourable to the development of the pest, for within this period this fever had more than once committed great havoc in the same parish. It could not have been that the little community who were now suffering so severely from it were proof against it, for as the event proved they were only too susceptible. The very magnitude of the contrast between these many years of past entire immunity from fever, and present great prevalence of it is, surely, in itself, decisive of the question.

"But there was no need of travelling back in time to give point to this antithesis. At the very date when the events were occurring, all the elements of this contrast were present on the spot.

"I have already stated that before reaching cottages Nos. 1 and 2, the stream served the office in common sewer to some twenty or thirty houses higher up. But while in Nos. 1 and 2, and in the two cottages *below* them, nearly every inmate was stricken with fever, in not one of the thirty houses above these, was there, from first to last, a single case.

"*It was down the stream that the seeds of the plague flowed.* Higher up, the stream was common sewage only; lower down, it was sewage *plus* the specific excreta of the fever patient. Hence the cardinal difference in the fate of those who were exposed to its emanations in the two situations.

"The only inference that it seems possible to draw from these facts is, that while sewage charged with the specific fever-poison is all-potent in breeding fever, sewage not so charged has no power to breed it at all." (*Typhoid Fever*, by William Budd, pp. 75-81.)

It would no doubt be possible to state a case against Budd's conclusions, indeed Murchison did so, but the reader will probably agree that Budd's method of setting out an inductive argument is admirable. Budd's work was, however, immediately noticed by Simon. In Simon's first report as Medical Officer to the Privy Council (written in 1859), his conclusion respecting the aetiology of an outbreak of typhoid in Windsor was as follows (the italics are in the original):

*"The System of sewerage at Windsor, with frequent domestic defects of sink-trapping, favoured the habitual escape of sewer-atmosphere into houses;*

*last year, from accidental circumstances, the sewer-atmosphere was at about its maximum of poisonousness; and the result was an epidemic of typhoid fever."*

In the third report, however (written in 1861), Simon inserted a footnote warmly commending Budd's researches.

"His [Budd's] arguments are also, I think, cogent to this general effect—that specially the bowel-discharges of the disease are means (yet not therefore necessarily the sole means) by which a patient whether migrating or stationary, can be instrumental in spreading the infection of typhoid fever. Provisionally these conclusions must be acted upon in their present unqualified form. But doubtless it is of practical importance to learn as exactly as possible, whether it is in all states and under all circumstances, or only in certain states and under certain circumstances, that the bowel-discharges of typhoid fever can effect what is here imputed to them." (Third Report, p. 2.)

The *specific* element of the aetiology, which was the essence of Budd's work, did not actually dominate the philosophy of epidemiologists; pragmatically, they held fast to the notion that the enteric group depended upon "filth," and the following quotation from Simon's report in 1874 is a succinct account of the philosophy which inspired all epidemiological work in England fifty to sixty years ago.

"Since the year 1849, when Dr. (now Sir William) Jenner made known his conclusive and masterly discrimination of this specific form of fever, successive studies have tended with singular uniformity to connect it in regard of its origin with nuisances of an excremental sort. In illustration of that fact in the natural history of enteric fever, I may refer to an abstract which I append of the experience of the Medical Department during the four years 1870-3 in this particular branch of disease-production: and such illustrations might be multiplied to any desired extent. The experience is, not only that privies and privy-drainage, with their respective stinkings and soakings, and the pollutions of air and water which are thus produced, have in innumerable instances been the apparent causes of outbreaks of enteric fever, but, further, that they have seemed capable of doing this mischief in a doubly distinctive way: first, as though by some aptitude which other nuisances of organic decomposition, though perhaps equally offensive, have not seemed equally or nearly equally to possess; and secondly, as though this specific property, so often attaching to them in addition to their common septic unwholesomeness, were not, even in them, a fixed property. The explanation of this experience, the explanation of the frequent but not invariable tendency of privy-nuisances to infect with enteric fever has

seemed to consist in the liability of such nuisances to carry with them, not invariably, but as frequent accidental adjuncts, the 'specific' contagium of any prevailing bowel-infection: for presumably the privies of a population receive (*inter alia*) the diarrhoeal discharges of the sick; and it has long been matter of fair pathological presumption that in any 'specific' diarrhoea (such as eminently is enteric fever) every discharge from the bowels must teem with the contagium of the disease. Medical knowledge in support of this presumption has of late been growing more positive and precise; and at the moment of my present writing I have the gratification of believing that under my Lords of the Council it has received an increase which may be of critical importance, in a discovery which seems to give us for the first time an ocular test of the contagium of enteric fever: in the discovery, namely, of microscopical forms, apparently of the lowest vegetable life, multiplying to innumerable forms in the intestinal tissues of the sick, penetrating on the one hand from the mucous surface into the general system of the patient, and contributory on the other hand, with whatever power they represent, to the bowel contents which presently have to pass forth from him. Adverting then summarily, in an administrative point of view, to the present state of medical knowledge and opinion as to the way in which enteric fever spreads its infection in this country, I would say that it is difficult to conceive, in regard to any causation of disease in a civilized community, any physical picture more loathesome than that which is here suggested: that apparently, of all diseases which are attributable to Filth, this, as an administrative scandal, may be proclaimed as the very type and quintessence: that, though sometimes by covert processes which I will hereafter explain, yet far oftener in the most glaring way, it apparently has an invariable source in that which of Filth is the filthiest: that apparently its infection runs its course, as with successive inoculations from man to man, by instrumentality of the molecules of excrement which man's filthiness lets mingle in his air and food and drink." (Report for 1873, pp. 13-14.)

I have quoted the whole of this passage because one cannot understand the development of any human knowledge, or policy based upon knowledge or belief, without a sense of *atmosphere*. That is true of the science one might suppose freest from the atmosphere of human emotion, pure mathematics; one will do James Bernoulli more (or less) than justice by reading his theorem only in a textbook. How much more important must atmosphere be in our subject. The reader can say with truth that there is more emotion than reason in Simon's statement; there is: just as there is in what we all say and write. But the student can probably see now what I meant by saying that, as a scientific man, Farr was greater than Simon, but that Simon

was a great administrator. The pragmatic theory of epidemiology in this field was, then, that outbreaks of typhoid were always due to the contamination of air, water, or other food by filth, and, since water was the most obvious source of bulk contamination *capable of safeguarding*, it was to water-borne typhoid that most attention was devoted. It might fairly be said that when an outbreak occurred, the local water supply was not in the position which the theory of our law assigns to an accused person, viz. that he is innocent until proved guilty, but in the position of being presumed guilty unless its innocence could be made to appear. I dwell a little upon this because, as we shall see, evidence of a different epidemiological chain of events has always encountered some prejudice and been more sharply criticized (when it has not been wholly ignored) than would have been the case if the atmosphere had been different.

It will be best now to examine carefully the kind of evidence upon which water has been convicted, and, with that object, I shall discuss two great epidemics, which, although they occurred a generation later than the time of which we have been speaking, typify the method of investigation, viz. the epidemic at Maidstone in 1897 and that at Worthing in 1893. At the time of the events we are to consider, Maidstone, the county town of Kent, was a thriving market town of nearly 34,000 inhabitants, and, in the ten years before 1897, both its general death-rate and its specific death-rate from typhoid compared favourably with those of England and Wales. In the week ending September 11, 1897, two cases of typhoid fever were notified, in the following week the number increased to one hundred and twenty-eight, in the week ending September 25th, five hundred and forty-four cases were returned, and the epidemic ran through the stages set out in Table 17.

Between August and January 1,938 persons were attacked and 132 persons died; in numbers of cases this is the largest modern explosive epidemic recorded in an English town, although that of Worthing caused relatively more cases, and both absolutely and relatively many more deaths.

The explosive character of the outbreak was taken to indicate that it depended upon a synchronous distribution of infective material to a large number of persons; the most obvious means

of such distribution are, if we exclude a miasmatic origin (*vide infra*), water and milk, and actually the inquiry was conducted

TABLE 17

## WEEKLY TABLE OF ATTACKS AND NOTIFICATIONS

Week ending	Borough of Maidstone, Exclusive of the Asylum		County Asylum		Rural District of Maidstone
	Notifications	Attacks*	Notifications	Attacks*	Notifications
August 28th ..	—	4	—	—	—
September 4th ..	—	29	—	—	1
September 11th	2	165	—	1	0
September 18th	128	434	—	18	2
September 25th	544	432	50	48	17
October 2nd ..	529	274	0	12	6
October 9th ..	246	134	39	15	8
October 16th ..	116	64	9	4	4
October 23rd ..	61	45	2	2	3
October 30th ..	44	33	0	4	1
November 6th ..	34	25	2	2	1
November 13th	22	23	4	1	0
November 20th	20	19	1	—	2
November 27th	15	13	—	—	—
December 4th ..	11	4	—	—	—
December 11th	7	5	—	—	—
December 18th	4	3	—	—	—
December 25th	0	2	—	—	—
January 1st ..	3	3	—	—	—
Totals ..	1,786	1,711	107	107	45

\* Although "Attacks" are not defined in the report, they are presumably "Notifications" respecting which enough information was available to enable the onset of illness to be dated.

(Taken from *Epidemic of Typhoid Fever, 1897, Borough of Maidstone*, L.G.B. Report, 1897, Table 1, p. 12.)

much like a trial with the water supply as the accused person.

The following is an outline of the case for the prosecution. It was shown that the catchpit of one of the springs forming

part of the town water supply was situated in a field liable to faecal contamination, and that such contamination by members of an encampment of hop-pickers had taken place. Samples taken from this supply yielded more albuminoid ammonia and oxidized nitrogen than what was deemed by the chemists of the period a "good water" should contain. When the incidence of typhoid upon houses receiving their water from different sources was compared, the following were the results. It appeared that two sources, the Cossington and Boarley supplies, served respectively 671 and 1,410 houses containing 3,355 and 7,050 persons; the house attack-rates were 2·8 and 4·46 per cent, the person attack-rates 0·86 and 0·97 per cent. The supply which included water from the impugned springs (Farleigh supply) was served to 3,916 houses containing 19,580 persons; 1,077 houses and 1,583 persons, percentages of 27·5 and 8·08, were attacked.

Of the public institutions of Maidstone, the County Asylum received the Farleigh supply, the barracks and the prison the Boarley or well water. In the asylum 107 cases occurred (among 1,600 patients and 130 attendants), in the barracks (population 300) and the prison (average population 171) none. Finally, of 13 cases notified from an extra-urban district, 11 occurred in houses supplied with the Farleigh water.

The case for the defence was founded upon the admitted fact that the drainage system of Maidstone was defective; a leading witness, the late Professor Corfield, adopting a variant of the so-called ground water theory—which we shall have to consider later on—urged that although the bulk of the cases had certainly occurred within the area of the Farleigh supply, that fact was not inconsistent with the theory that the epidemic was due to the defects of the drainage, for the Farleigh supply covered the highest parts of the town, and the ill effects of badly flushed drains and imperfect ventilation would be at first most felt at the highest points.

It was urged: (1) That although most of the cases were within the area of the Farleigh supply, many actually occurred outside and could not be presumed to have arisen from consumption of Farleigh water. (2) That no less than three hundred and fifty-seven cases occurred sixteen or more days after the water from the impugned source had been entirely excluded from the supply,

that evidently these attacks could not have been due to the water, and that the factors producing them might reasonably be supposed to have operated before and perhaps have been responsible for the earlier cases.

To a later generation these contentions, which were not

TABLE 18

## DEATHS FROM TYPHOID IN MUNICH

Year	Inhabitants	Annual Number of Deaths	Per 100,000 Inhabitants	Year	Inhabitants	Annual Number of Deaths	Per 100,000 Inhabitants
1851	123,957	123	99	1874	181,300	289	159
1852	125,588	152	121	1875	187,200	227	121
1853	127,219	235	184	1876	193,024	130	67
1854	128,850	293	227	1877	205,000	173	84
1855	130,481	253	193	1878	211,300	116	55
1856	132,112	384	291	1879	217,400	236	109
1857	133,847	390	291	1880	223,700	160	72
1858	135,733	453	334	1881	230,028	41	18
1859	137,005	240	175	1882	236,400	42	18
1860	140,624	153	109	1883	242,800	45	19
1861	144,334	172	119	1884	249,200	34	14
1862	148,200	300	202	1885	255,600	45	18
1863	154,602	252	163	1886	262,000	55	21
1864	160,828	397	247	1887	268,400	28	10
1865	167,054	338	202	1888	292,800	31	10.5
1866	168,265	342	203	1889	306,000	31	10.1
1867	169,476	88	52	1890	331,000	28	8.5
1868	172,688	136	80	1891	357,000	24	6.4
1869	170,000	190	111	1892	372,000	11	3.0
1870	170,000	254	149	1893	385,000	57	14.8
1871	170,000	220	129	1894	393,000	10	2.5
1872	169,693	407	240	1895	400,000	15	3.7
1873	175,500	230	131	1896	412,000	14	3.4

(Taken from von Pettenkofer's *Munich a Healthy City*, up to 1887 inclusive; after 1887 from returns obtained from the Statistical Bureau. Published also in "The History of Typhoid Fever in Munich," *Trans. of the Epidem. Society of London*, Vol. XVIII, 1897-8, Table I, p. 42.)

accepted by the presiding inspector at the inquiry (the late Dr. Theodore Thomson), will seem trivial. They are really worthy of more consideration than the reader may suppose, and I must give an outline of some evidence fresh in the memories of epi-

miologists of thirty years ago but now almost forgotten. In the city of Munich the incidence of fatal typhoid declined very greatly in the last fifty years of the nineteenth century, and the epidemiology of the prevalences was investigated by von Pettenkofer.

The city stands upon a bed of gravel underlying which is an impermeable layer of marl; between the marl and gravel flow the subsoil waters. From 1858 onwards improvements were made in drainage; Munich began as a town of privies and cesspools, by the end of the century most of the cesspits were gone and an adequate system of sewerage had been introduced. In 1878 some eight hundred slaughter-houses within the city, most of which drained into the soil, were removed and replaced by a properly drained slaughter-house outside the city.

Down to 1865 the city was supplied with drinking water from the subsoil water. In 1865 a considerable new supply was added to the southern and western areas of the city derived also from subsoil water, but taken in an uninhabited area above the city. Finally, in 1883 a new supply, derived from springs impounded in a valley of the Bavarian Alps twenty miles away, was provided. Pettenkofer, who began his studies in 1854, started with a presumption against the water supplies, which, he was able to show, were certainly often heavily contaminated with organic matter, but in no instance could he obtain any evidence of the kind relied upon in the inquiry we have just examined, viz. of a spatial or temporal correlation between incidence of cases and use of a particular water supply. He did, however, find a fairly regular correlation between increasing prevalence of typhoid and a rise in the level of the ground water. He noted that down to 1883 the population was drinking nothing but subsoil water, but that over this period the prevalence of typhoid was declining and the drainage of the soil improving. Upon this basis was founded the localist doctrine, viz. that epidemic typhoid requires three conditions: (1) the presence of a specific agent in the soil; (2) a general pollution of the soil, together with certain conditions of porosity affected by temperature and moisture, or oscillations of the subsoil water; (3) predisposition of the inhabitants. So expressed, the hypothesis does not shock any of our prejudices. It would be hard for the reader (or for me) to stomach the view that sewer gas could "give" one typhoid, much less hard to

suppose that the emanations of a polluted soil might lower resistance so that, given the presence of a specific agent, a prevalence might be generated.

Such, I think, were the considerations which led the inspector

TABLE 19

SHOWING FORTNIGHTLY, FROM MARCH TO DECEMBER 1893, THE NUMBER OF CASES OF ENTERIC FEVER NOTIFIED IN "WORTHING," "WEST WORTHING," WEST TARRING, AND BROADWATER

Period	"Worthing" (Population 15,317)	"West Worthing" (Population 2,116)	Village of West Tarring (Population 1,070)	Village of Broadwater (Population 787)
Month of January .. ..	1	—	—	—
Month of February .. ..	1	—	—	—
Month of March .. ..	—	—	—	—
April 1st-14th .. ..	—	—	—	—
April 15th-28th .. ..	—	—	—	—
April 29th-May 12th .. ..	40	—	1	1
May 13th-26th .. ..	189	—	—	2
May 27th-June 9th .. ..	55	—	—	—
June 10th-23rd .. ..	12	—	—	2
June 24th-July 7th .. ..	146	1	3	4
July 8th-21st .. ..	418	4	3	18
July 22nd-August 4th .. ..	151	7	8	1
August 5th-18th .. ..	120	27	25	8
August 19th-September 1st	43	6	7	1
September 2nd-15th .. ..	27	7	1	—
September 16th-29th .. ..	31	2	1	—
September 30th-October 13th	8	1	3	1
October 14th-27th .. ..	9	—	1	—
October 28th-November 10th	6	—	1	—
November 11th-24th .. ..	2	3	1	3
November 25th-December 8th	—	—	—	—
Total .. ..	1,259	58	55	41

(Taken from Report of Medical Officer L.G. Board, 1893-4, Table V, p. 51.)

in the Maidstone case to attribute quite considerable weight to the contention that, apart from water pollution, soil contamination in Maidstone was an important if secondary factor.

Before we discuss whether the judgment—"On a review of the whole evidence, we have no hesitation in coming to the conclusion that the epidemic was caused by the pollution of the water sup-

plied by the Maidstone Company from their Farleigh sources"—was logical, let us examine the evidence in another even more dramatic case, that of Worthing.

The site of these events is, for reasons which will appear, divided into four aggregations: the town of Worthing separated into "Worthing" with 15,317 inhabitants, "West Worthing" with 2,116, and the adjacent villages of West Tarring (1,070) and Broadwater (787).

Between April 1893 and January 1894, 1,411 of their inhabitants fell sick of typhoid and 198 died of it. The space and time distribution of the cases is shown in Table 19.

It will be observed that in "Worthing" the time-distribution has two peaks, the first between May 13th and 26th, the second, much taller, peak eight weeks later. "West Worthing" and West Tarring have single peaks both later than the second peak of "Worthing," Broadwater a peak coincident with the second Worthing peak. The next Table (p. 153) distributes the cases by date not of notification but of attack, but does not sensibly modify the comparison.

This was the time-distribution. With respect to space-distribution within the areas, a series of fortnightly spot-maps—too numerous to reproduce—suggested that although in "Worthing" and Broadwater the scatter of cases was fairly uniform, in "West Worthing" and West Tarring the cases were clustered around particular points.\* For instance, in West Tarring a group of streets housing less than two-thirds of the population contributed fifty-one of the fifty-five cases.

The conclusion was drawn that "West Worthing" and West Tarring on the one hand and "Worthing" (so far as concerned its second phase) and Broadwater on the other formed similar epidemiological groups. The inquiry next deals with common factors. No statistical evidence of correlation between the distribution of milk supplies and of cases of typhoid was obtained. With regard to sewerage, there was again lack of correlation; in the words of the inspector (Dr. Theodore Thomson): "In short, the behaviour of the disease generally is opposed to any probability of sewer infection as a cause. Its behaviour in 'Worthing' was similar to its behaviour in Broadwater village, and yet the

\* Insufficient detail is provided to admit of close examination.

'Worthing' sewers do not extend into Broadwater village, which is, as has been said, wholly without sewers. In 'Worthing' and West Tarring, again, there were striking differences in the manner of rise and progress of the fever, notwithstanding that these places

TABLE 20

SHOWING THE NUMBER OF ENTERIC FEVER ATTACKS ASCERTAINED TO HAVE COMMENCED IN EACH FORTNIGHT FROM MARCH TO DECEMBER 1893, IN "WORTHING," "WEST WORTHING," WEST TARRING, AND BROADWATER

Period	"Worthing" (Population 15,317)	"West Worthing" (Population 2,116)	Village of West Tarring (Population 1,070)	Village of Broadwater (Population 787)
The month of January ..	1	—	—	—
The month of February ..	1	—	—	—
The month of March ..	—	—	—	—
April 1st-14th ..	—	—	—	—
April 15th-28th ..	9	—	—	1
April 29th-May 12th ..	153	—	1	2
May 13th-26th ..	106	—	—	—
May 27th-June 9th ..	24	—	—	2
June 10th-23rd ..	59	—	—	—
June 24th-July 7th ..	391	4	6	12
July 8th-21st ..	225	2	3	12
July 22nd-August 4th ..	110	24	21	4
August 5th-18th ..	78	11	14	4
August 19th-September 1st	30	4	2	—
September 2nd-15th ..	41	9	1	—
September 16th-29th ..	10	—	2	—
September 30th-October 13th	6	1	5	1
October 14th-27th ..	9	—	—	2
October 28th-November 10th	5	2	—	1
November 11th-24th ..	1	1	—	—
November 25th-December 8th	—	—	—	—
Total .. ..	1,259	58	55	41

(Op. cit., Table VI, p. 52.)

have a common sewerage system. In 'West Worthing,' moreover, which has its own separate sewerage system, the disease behaved quite otherwise than in 'Worthing,' and instead closely followed the course taken by it in West Tarring, which is, as already stated, on the same sewerage system as 'Worthing.' In view of these facts, it becomes apparent that a sufficient explanation of the

cause of the outbreak of enteric fever in these four places is not to be found in infection propagated by emanations from sewers."

We now come to the third communal factor, the water supply. The "Worthing" supply was a public service derived from deep wells driven into the chalk, and, as the population grew, new shafts were sunk. Already in 1885 difficulties were encountered owing to the leaking of water before the chalk was reached. Finally, in 1893 it became necessary to drive a new heading from the bottom of an existing well, which work began on March 13th. From the beginning small fissures were encountered, and on April 14th a large fissure was cut into, estimated to yield more than 2,500 gallons a minute. So sudden was the inrush that the workmen had to abandon their tools and fly for their lives. This water supply was also distributed to Broadwater. But "West Worthing" and West Tarring received a wholly different supply, derived from two wells in the chalk. Respecting this supply no incidents of the kind mentioned above are narrated. In all four areas local wells (mostly shallow and dry stined) were in use and were relatively important in Broadwater (126 inhabited houses took well water, 65 the "Worthing" service) and West Tarring (60 houses on well water, 169 on "West Worthing" service). In "Worthing" only 31 out of 2,890 houses, and in "West Worthing" 21 out of 347, were so supplied. It was found that in Broadwater, while 19 of the houses (65) on the "Worthing" municipal supply had cases of enteric, only 12 of the 126 having well water were infected. When individuals were considered, it appeared that only 6 of the 41 Broadwater patients had not drunk, at some relevant time, "Worthing" water. Chemical and bacteriological (the latter, judged by present-day standards, inadequate) evidence of organic and bacterial pollution of the "Worthing" water was furnished. The inspector accordingly concluded that:

"The chain of evidence against the 'Worthing' water is complete. It has been shown that the epidemic of enteric fever in 'Worthing' and Broadwater was intimately related in point of time to the admission to the 'Worthing' service of water from a new source of supply; that thereafter the disease became general throughout the areas supplied by this service; and that within the limits of these areas the incidence of fever was almost wholly on houses supplied by this water. Further, it has been shown that certain apparent exceptions to this rule, were, for the most part, persons who had elsewhere consumed the water in question. And now

it appears not only that this new source of water supply was open to dangerous contamination, but also that, by the aid of bacterioscopic examination, demonstration is forthcoming of such contamination having actually occurred."

The reader cannot fail to be impressed by the elegance of this demonstration; it is as neat as anything due to the late "Mr. Sherlock Holmes" or to "Dr. John Thorndyke"—still happily with us. But there remain pieces of the epidemiological puzzle not fitted in, viz. the prevalences in "West Worthing" and Tarring. Here the patients had not consumed the peccant "Worthing" water. No connection between the July (and later) series and antecedent cases, whether in "Worthing" or elsewhere, was made out, milk and general sanitary conditions (sewer "emanations") had been dismissed without any stains upon their respective characters, and nothing whatever was known to the prejudice of the local water supply. *Que faire?*

We have seen that the scatter of cases in "West Worthing" and West Tarring was not, as in "Worthing," indiscriminate. Therefore (if, of course, we have made up our minds that water was responsible) "there is almost involved a presumption that this water supply became contaminated after withdrawal from its source: namely, in the mains of the water company."

The inspector found the following support of the presumption. He noted that the infected areas of "West Worthing" and West Tarring were below the level of a ridge, and the mains so situated that if the street hydrants fitted to the "West Worthing" mains were liable to regurgitation (which, he found, they were), then if the streets were watered with contaminated water the mains might become infected by gravitation. The suggestion was indeed made that the outbreak was due to the watering of "West Worthing" streets with "Worthing" water during some days of July or August 1893. But—with very natural regret, for such a concatenation of events would be almost too beautiful to be true—the inspector held that this charge was unproven, although on balance he decided to convict the "West Worthing" mains. It is rather hard not to feel that this "West Worthing" sequel makes the parallel with the exploits of Mr. Holmes and Dr. Thorndyke uncomfortably complete. One recalls the—indubitably sound—aphorism of Mr. Holmes that having excluded all other possible

explanations, what remains, however improbable, must be true. Indeed, it must, but one may doubt whether a trichotomy of milk, sewer emanations, and water *really* measures up not the fictitious universe of discourse but the wider field of epidemiological happenings. Statistically both here and at Maidstone correlation was identified with causation. We have our A's and

TABLE 21

ENTERIC FEVER, STANDARDIZED DEATH-RATES AT ALL AGES, 1870-1931

*England and Wales*

Period	Death-rate	Period	Death-rate	Period	Death-rate	Period	Death-rate
1870	385	1886	186	1902	126	1918	25
1871	368	1887	187	1903	101	1919	15
1872	376	1888	173	1904	93	1920	14
1873	380	1889	177	1905	90	1921	16
1874	365	1890	180	1906	92	1922	12
1875	369	1891	169	1907	68	1923	12
1876	308	1892	138	1908	75	1924	13
1877	277	1893	230	1909	60	1925	10
1878	304	1894	160	1910	53	1926	9
1879	229	1895	176	1911	67	1927	9
1880	270	1896	167	1912	44	1928	11
1881	212	1897	157	1913	41	1929	9
1882	232	1898	182	1914	46	1930	7
1883	221	1899	198	1915	37	1931	6
1884	239	1900	174	1916	29		
1885	178	1901	155	1917	26		

B's, the attacked and the (more or less) unattacked. Just as many A's as B's are *a*'s and are *b*'s, but many more A's than B's are *c*'s, *therefore*, since being an A could not make one a *c*, being a *c must* make one an A; which is the logic of "practical" men, but not of the Academy. But it is easy to cast stones, and certainly no additions to knowledge made since 1893 justify us in saying that the great epidemics of Worthing and Maidstone were *not* water-borne outbreaks. Again, however shaky the evidence of precise aetiology in detail, there is a time-correlation between falling mortality from typhoid and energetic water campaigning which is sufficiently impressive. In the above Table we have the rate of mortality from enteric fever from 1870 to 1931.

One notices on the chart (Graph 1) three phases; roughly from 1875 over the next ten years there is a rapid fall, then rather more than a decennium showing little change. At the beginning of the twentieth century another rapid fall began which slackened into a gentle descent which has continued fairly regularly since about 1910. The reader should remember



GRAPH 1.

that the eternal difficulty of comparability between diagnosed causes of death at different epochs probably tells against us and makes the general decline less impressive than it really is, because typhoid is now more freely diagnosed.

I think a pragmatist would interpret the time-sequence in this way. We have seen that from the 'fifties Simon waged a vigorous campaign against filth in general and filthy water in particular, and gradually means of coercion were given to the "bureaucrats." After 1875 something *had* to be done, sooner or later, even by the most thick-skinned local authorities, in areas where sewage

was used for drinking purposes. There was a vigorous overhaul of drains and water. Hence the first rapid decline of the typho-enteric group. Then came a period when the number of utterly detestable water supplies was, relatively to the whole number of supplies, so small (some existed and exist even to this day) that not much impression upon the *national* rates could be made by impeaching water and drains; there was an epoch of stagnation. Then a new gospel is vouchsafed, that of the "carrier" and the consequent importance of personal cleanliness as distinct from communal cleanliness. Another criminal can be placed in the dock, a real person this time, not a water company or a municipality. Some logicians, such as Sir William Hamer, have made endless fun of the evidence upon which the "carrier" has been convicted, and have professed to see the time when the segregation not of the "carriers" but of, it might be, the less numerous non-carriers would be the objective of a stage army of bandits termed bacteriologists (believed to have designs upon the Sleeping Beauty of Epidemiology, but unable to carry out those designs, for nobody, not even Sir William, knew just where the Beauty slept). The pragmatist, however, *ex post facto*, notes that the spread of the new gospel did coincide with a new downward plunge of the secular rate. The pragmatist would further remark that countries which were backward to campaign against filth were behind-hand in experiencing a decline of mortality from typhoid; he would ask, in vain, for a single instance of regular secular decrease in an urban community which had not campaigned against filth. From his point of view, the furious controversy between the followers of Pettenkofer and the followers of Koch would be mere logomachy: what *does* it matter whether the "filth" is in the soil or in the water supply?

I am a good deal of a pragmatist, but wear my pragmatism with a difference and hope to persuade the reader to do so too. We must, I think, agree that all attempts to prove that any one particular set of factors has been *the* "cause" of a particular prevalence have been logically unsatisfactory. I chose deliberately two of the most striking and "typical" water-borne examples to demonstrate this. It is equally easy to pick holes in the localist or soil doctrines. Take for instance the seemingly attack-proof argument of Pettenkofer for Munich. The late Professor Corfield,

who was very far from being a bigoted smeller-out of water epidemics—he was a witness for the defence of the incriminated Maidstone water—commented upon the Munich evidence thus:

“This diminution was produced by the purifying of the subsoil, by making cesspools water-tight, by extending the system of sewerage, and, finally, by the sudden abolition of the eight hundred slaughter-houses in the city in 1878. It is quite obvious that purification of the subsoil must have been attended by considerable purification of the water of the wells by which the town was supplied ‘until 1883, three years after the epidemic waves had ceased when the high land water-supply was introduced. This supply has gradually been distributed to the whole city.’ I cannot help thinking that the drinking water in Munich had more to do with the prevalence of typhoid fever there than Pettenkofer thought was the case.” (Corfield, *The Aetiology of Typhoid Fever*, London, 1902, p. 120.)

In other words, the failure of the method of overt correlation in space or time was *not* conclusive evidence that the water was wholly innocent, any more than the presence of such correlation is conclusive evidence that water is guilty.

There is a further point to be noted. Explosive epidemics of typhoid occur the evolution in time of which resemble quite closely that of Maidstone, and yet the pollution of a communal water supply can be excluded. Severin recently described two instructive examples. The first concerned a colony of German ranchers in Santa Catharina, in Brazil, the other a colony of some 650 families of Brazilian born Italians in Viaductos. Both epidemics were severe; in the former there were 190 cases with 17 deaths, in the latter 680 cases with 130 deaths. The German colonists were badly housed and fed, but civilized people; the inhabitants of Viaductos were economically better placed, but their cultural level was almost unbelievably low, and they set all rules of hygiene and personal cleanliness at defiance. In neither community was there any question of the pollution of a common water supply for the simple reason that none existed. In both some favourable concurrence of many factors must have been responsible for the explosions. The inference is, of course, not that our judgments in the Maidstone and Worthing cases were wrong, but that there are no hard-and-fast simple criteria the application of which will enable us to reach truth easily. We can never expect to reach more than probable conclusions; in epidemiology there are *no*

crucial cases. Most of the controversial literature respecting the typhoid group of crowd-sicknesses owes its production to a desire, natural enough, for simplicity. Each party wishes to prove that the truth it sees is the whole truth. As the man in R. L. Stevenson's anecdote remarked, there is no such thing as the whole truth. This, however, may be believed without much risk of error, that the practical campaign begun by Simon more than sixty years ago was planned on sound lines, and that the orthodox hygienic teaching of sanitarians on the typhoid group is sound. In an urbanized state, unsleeping vigilance with respect to the communal food supplies, before all the water supplies, and unwearied inculcation of personal cleanliness are the best means of protection. Lest we should flatter ourselves that all this is a commonplace of modern administration, I remind the reader that since the war two serious outbreaks of water-borne enteric fever have occurred in this country, that in Bolton-upon-Deane in 1921 and that in Malton in 1932. In the former epidemic there were 397 cases with 45 deaths, in the latter 270 cases with 23 deaths.

Bolton-upon-Deane is in the West Riding of Yorkshire; five adjoining areas were involved: the urban district of Bolton-upon-Deane, the urban district of Darfield, and the parishes of Great and Little Houghton and Billingley; the respective populations were 11,947, 5,566, 2,292, 522, and 170. In the ten years before the outbreak only 38 cases of enteric fever had been notified in the whole area, 25 of these in Bolton-upon-Deane and 11 in Darfield. The 1921 events occurred in two series. The first, contributing 137 cases, began in the week ending July 23rd with 7 notifications, 5 in Bolton-upon-Deane and 2 in Darfield; the maximum was 19 in the following week, and the distribution over the area was fairly uniform. The second series was confined to the village of Bolton-upon-Deane, one of the villages within the Bolton-upon-Deane urban district. It began in the week ending October 8th with 2 cases, in the successive weeks there were 17, 57, 58, 53, 33, 16, 14, 2, 6, 1, 1; in all 260 cases. In the whole epidemic series there were 397 cases with 45 deaths. In the first series 2·3 per cent of houses of the area had cases and 24·5 of the attacked houses more than 1 case. In the second, limited to Bolton-upon-Deane village, 20 per cent of the houses were attacked, and in 42·6 per cent of these houses there were

more than 1 case. All the areas (colliery villages) were sewerred, but a number of privy middens still existed. Originally the water supply was obtained by pumps from shallow wells sunk in the sandstone; such wells still existed and were in use in the village of Bolton-upon-Dearne, but hardly elsewhere except to a slight extent in Great and Little Houghton and Billingley. In 1875 a company began to deliver a piped supply from a deep well, and subsequently other supplies were taken into use and the supplies consolidated in 1920. The circumstances of the first outbreak were these, a common factor was the supply of water by the consolidated undertaking from a source obtained from the Dearne Valley colliery. A specimen of this water "showed a certain amount of pollution, and the presence of streptococci would make one suspicious of human excrement." No satisfactory evidence was obtained as to how the supply became contaminated. It appeared that during the coal strike in April-July 1921 many persons raided a wood for fuel, which wood was situated on sandstone overlying the coal measures; this was fissured and pollution possible (similar story to Maidstone). In the second outbreak, the infected area was inadequately supplied always from the piped supply, and it was actually cut off altogether on September 27th and October 3rd. Resort was had to a public pump drawing water from a shallow well in the sandstone rock. There were also prejudices against the piped supply, which had been chlorinated. The season had been dry, probably the pump drew on a wider area than usual, and it was subsequently found that the lowest part of a quarry and also the floors of various midden privies were above the bottom of the well. Two cases of enteric were discovered in the quarry workers. Children playing and an entertainment called the Bolton-upon-Dearne feast on August 13th to 20th were also possible sources of pollution (one child who played certainly and one of the showmen's children possibly had enteric). The quarry was fouled with excrement.

The general findings were these. The piped water supply was (like the Maidstone supply) inadequately safeguarded and liable to casual contamination. The first and less severe outbreak was due to this. The second outbreak occurred among persons who, to a greater or less extent, used a water supply liable to gross contamination. During the first outbreak the users of that water

escaped altogether. The first outbreak, however, afforded abundant material for contamination of the soil and then the users of the well water suffered very severely. (Cf. the case of Terling in Essex sixty years ago.)

The Malton epidemic, which involved an old market town in the North Riding of Yorkshire, is a good example of circumstantial evidence. Down to September 23, 1932, there was no known case of enteric fever in the district; on that day a patient was admitted to the Public Assistance Institution and on September 26th he was diagnosed to be suffering from enteric fever. The patient was not removed to an isolation hospital for more than a month. In the meantime his excreta passed into the common sewer of the town by way of a broken drain which allowed part of its contents to soak into the surrounding soil, polluting it heavily. In this way the water supply of the town became infected and the epidemic followed. The water supply of the town was derived from a local well, the abandonment of which, owing to its liability to pollution and to an associated high incidence of diseases of the enteric group, had been urged on the local authority by the Local Government Board forty years ago. Two generations after Simon's campaign there are still some local authorities not wholly undeserving the lash of his rhetoric.

The largest example of a milk-borne epidemic in recent English experience occurred in the urban district of Epping (Essex). In the first months of 1931, between January 28, 1931, and February 21st, 260 cases of paratyphoid are known to have occurred, 200 of these in the small town of Epping with a population of rather more than 4,000. The age and sex incidence of these cases is shown in the Table on page 163.

Seven of these cases were fatal.

Sixty-seven per cent of the cases were of persons under twenty-one. In Epping, excluding 33 cases in the Poor Law Infirmary, the house incidence was as follows: there were 112 houses each with a single case, 18 houses with 2 cases, 5 houses with 3 cases each, and 1 house with 4 cases.

All the victims had consumed milk from one source of supply (which source cannot, *at most*, have supplied more than half the inhabitants of the town, as its estimated number of consumers both within and without Epping was 2,500, and a considerable

proportion of the milk went out of the district). Further, 25 cases occurring in the borough of Walthamstow were all of persons who had consumed the suspected milk, likewise 2 cases in the urban district of Chingford were of consumers of this milk. The incidence of the disease, therefore, upon the consumers of the suspected milk was so great that the likelihood of its production by the play of mere chance was very small. It was also found that an employee on the farm had, at relevant times, been suffering from paratyphoid infection.

The indirect interest of this outbreak is perhaps greater than

TABLE 22

Age	Males	Females
0-5	25	29
6-10	31	24
11-15	18	14
16-20	15	19
21-30	12	17
31-	15	41
Total ..	116	144

its direct interest. In the effluent of a sewage works dealing with the excreta of the town during the epidemic, *B. paratyphosus B* was discovered. This effluent discharged into a brook, the contents of which might and probably did form part of the London water supply. Very energetic measures were taken; both the brook and stored water were chlorinated, and no cases of paratyphoid in the metropolitan area could be traced to this source of infection.

The epidemic itself is a sufficiently typical example of milk-borne infection and illustrates the kind of statistical evidence upon which judgment must be based, viz. the correlation in space between the occurrences of disease in milk consumers and the use of the milk, and in time between the presence of means of infection on the farm and realized infection in consumers. The age distribution again shows a bias towards the young, i.e. towards heavy consumers of milk.

I think that the story told in this chapter justifies the optimism

I displayed at the beginning of it, that we may fairly regard the course of events as a sanitary triumph. But two of the three outbreaks described in the last pages are sufficiently impressive warnings that danger still lurks in wait, that, in this matter of enteric diseases, central and local health authorities can never afford to relax their vigilance. Here, if anywhere, we should applaud the strictest observance of sanitary law, we should not be ashamed of belonging to the strictest sect of pharisees.

#### RECOMMENDATIONS FOR FURTHER STUDY

Let it be said here, and once for all, that Creighton's *History of Epidemics in Britain* and Hirsch's *Handbook of Geographical and Historical Pathology* should be read and re-read by anybody who wishes to be an epidemiologist. Many of the conclusions drawn in both books are now known to be either erroneous or incomplete, but neither book will ever be out of date. Creighton's book can be read with pleasure and profit, Hirsch's book with profit.

Passing to the special subject of the chapter, Jenner's classical study is reprinted in *Lectures and Essays on Fever and Diphtheria*, London, 1893; Budd's in his *Typhoid Fever: its Nature, Mode of Spreading and Prevention*, London, 1873. F. P. Gay's *Typhoid Fever*, New York, 1918, contains a very good historical summary and an excellent bibliography of the subject. Reports on all the English epidemics I have discussed will be found in the official publications of the Ministry of Health or its predecessor the Local Government Board. The best accounts in English of recent epidemics abroad are those of Dr. Stallybrass in his treatise *The Principles of Epidemiology and the Process of Infection*, London, 1931. While this book was being printed, *Some Notable Epidemics*, by H. Harold Scott (London, 1934), was published. This excellent book contains full accounts of epidemics discussed in this and later chapters, and will save the students frequent references to official reports.

## II

### CHOLERA

THERE is an analogy between this group and the typhoid group of crowd sicknesses. The biological phenomena of both are largely determined by intestinal lesions, and, in the opinion of most sanitarians, a contamination of the food or drink of the community or of groups of it is the primary aetiological factor. But there are great contrasts. As an epidemiological phenomena cholera is much more dramatic and also, from the point of view of Western Europe, much more exotic than the continued fevers. "The Indian or Asiatic cholera," wrote Creighton, "which first showed itself on British soil in one or more houses on the Quay of Sunderland in the month of October 1831, was a 'new disease' in a more real sense than anything in this country since the sweating sickness of 1485." Creighton was, of course, familiar with the clinical analogies between *cases* of Asiatic cholera and *cases* of acute bowel complaints long endemic; he was referring to the epidemiological features of the great pandemics which at various intervals since 1817 down to a time within living memory have ravaged parts of Western Europe. His own epidemiological doctrine—a slight modification of Pettenkofer's—differed widely from what is now orthodox faith.

*Cases* of cholera in its deadly form were accurately described in the Hippocratic collection; epidemics of cholera occurred, for instance, in Alkmar in 1548, in Nîmes in 1645, in London in 1669 and 1676, in Vienna in 1786, before the nineteenth century. But epidemiologists agreeing in little else agree that the particular manifestations of cholera which showed themselves in Europe after Waterloo differed epidemiologically from anything which had been seen before. This difference may be summarized in a phrase as a difference in *dispersiveness*. "What," writes Sticker, "was new in the history of Indian cholera [he is writing about the events of 1817] and rightly caused apprehension there as well as here was the further intelligence that this destructive epidemic no longer confined itself to a particular area and at the accustomed season of the year appeared simultaneously in several

places, but set itself in motion, under the influence of some mysterious impulse began to travel, and, without paying attention to the season of the year, attaching itself to the lines of human intercourse, spread widely in various directions, exacting everywhere hecatombs of victims. In that very year a great part of the peninsula was conquered; in the following year cholera crossed the frontier of upper India and travelled east and west through the northern lands of Asia. By 1823 cholera, in the Caucasus and on the Volga, reached the frontiers of Russia, and thus menaced Europe.”\*

The objective facts are simple enough. The year 1815 was unusually wet in many parts of India and there was a general failure of the rice crop; 1816 was abnormally dry and warm, but the beginning of 1817 was again very wet, and, as in 1815, there was much flooding. In the wet May season cholera appeared, first in the northern provinces of Bengal, as it had often appeared before, but with the difference that not only the untouchables, but other castes and even Europeans, were stricken, and the sickness spread—not like the wind, no faster than the tempo of human travel, but spread ultimately over almost all India. From this time a world-wide dissemination began. Russia was reached after six years, but it was not until after the development of another wave of cholera in India herself that the outflowing tide reached the capital cities of Russia, in 1830-1. Westwards from Russia in a world of ships, even sailing ships, was a less leisurely journey, and England, as we have seen, was reached in October 1831. The first pandemic falls into two parts, from 1817 to 1823, when the confines of Europe were reached, and then from 1826 to 1838, within which termini almost all nations and peoples from 41 degrees south latitude to 65 degrees north latitude were affected. In 1838 the end came—indifferently, says Sticker—in places where quarantine and disinfections had been or had not been enforced.

The second pandemic, like the first, began in India; it lasted twenty years from 1840, reached Europe in 1847, remained in Europe some twelve years, and petered out in 1864.

The third pandemic lasted from 1863 to 1875: reached Europe in 1865 and took the front of the stage in 1866. In its first march

\* G. Sticker, *Abh. a. d. Seuchengeschichte*, II Bd., *Die Cholera*, Giessen, p. 9.

westwards cholera took twelve years to travel from India to Moscow; in its second pilgrimage it had followed largely the old land route, but had gone through Persia, Syria, Arabia, and by Bokhara and Orenburg to Moscow within a year. In the third migration the land route through Afghanistan, Persia, and Russia remained free; cholera came on shipboard to Suez and Egypt, and availed itself of the sea intercourse between the Nile delta and the Mediterranean ports to reach Europe. By 1869 the tide was ebbing and only a few foci retained expansive force—a recrudescence in 1871 affected Russia, Austria, and Germany, but failed to reach the northern lands. In 1875 the pandemic was over.

On November 16, 1869, the Suez Canal was opened for traffic, and it was naturally expected that the dangers of an extension of cholera to Europe would thereby be intensified. In 1870 only 26,758 passengers passed on shipboard through the Canal, but by the end of the nineteenth century the number had increased almost tenfold (252,694 in 1905). Actually, however, no case of cholera was seen in Europe or Egypt for eight years; the fourth pandemic began in 1881 and lasted for fifteen years. In comparison with its forerunners, this march was a much less vigorous affair. In 1881-2 cholera probably accompanied the Indian Mussulman pilgrims to Mecca. In the summer of 1883 cholera was epidemic in Egypt; on April 26, 1884, cholera reached Toulon, but in so mild a form as to be overlooked—it revenged itself in the following September. By the end of that month 280 administrative districts in 15 of the southern departments of France were involved; the cases were estimated at 10,000, the deaths at 5,000. The march did not continue northwards. In Italy, on the other hand, although there was no spectacular epidemic, there were about as many cases and deaths as in France. Spain suffered that year, and much more severely in the following year, 57,000 deaths and 160,000 cases. No further serious manifestations in Europe occurred until 1892. Then the path of extension seemed to be overland, and in August-November of that year the serious epidemic in Hamburg, with nearly 17,000 cases and 8,605 deaths, took place. England remained wholly unaffected by this pandemic.

A fifth pandemic period has been reckoned to begin in 1899, but from the north-west European point of view it has been

a small affair. Of course, if we choose to be strictly insular we may say that so far as home-keeping English are concerned, *Cholera asiatica* has been of no real interest for more than sixty years, but *some* epidemiological importance must be attached to the fates of those who have not enjoyed our sanitary blessings.

The 1899 march began to acquire European importance from the appearance of cholera in Dscheddah and Mekka. During the festival of February 1902 some 4,000 deaths are said to have occurred in Mekka; in Egypt 40,000 are said to have died in three months. In the following year Syria was involved and much of Asia Minor. In the spring of 1904 cholera came with caravans from Persia to Baku and gradually invaded Russia. In the wet summer of 1905 there was a remission, but in 1907-9 most of Russia was involved. In St. Petersburg there were more than 7,000 cases in 1909. In all Russia 1908 produced some 14,000 deaths. During this period West Europe was unaffected, and but few and scattered "cases" occurred in Germany. Italy alone (in the summer of 1911) suffered from seriously epidemic *Cholera asiatica*.

The relapse into barbarism of 1914 might have been expected to favour the diffusion of cholera, and, indeed, a considerable prevalence occurred in the eastern and south-eastern parts of Europe. Germany, Austria, and Italy all acquired cholera, ultimately from Russia, but, on the whole, cholera hardly assumed the importance which its past history entitled us to expect. Since the war cholera has as an epidemic phenomenon been confined to Asia. In 1921 India experienced a large epidemic, almost half a million cases were reported, a considerable epidemic in 1924 (more than 300,000 reported cases), and again in 1930 the prevalence was very large. Europe remains unscathed. Certain changes of religious opinion in the guardians of the sacred places of Islam in Arabia have, I understand, diminished the flow of pilgrims, and *pro tanto* relieved the apprehensions of the sanitary overseers of the pilgrim routes.

What one may call the philosophy of epidemic cholera has undergone many vicissitudes. Sixty years ago the Pettenkofer-Bühl doctrine was probably accepted by most scientific men. I have spoken of that general doctrine in discussing typhoid. I need only remind the reader that it gives to the soil an important rôle;

it does not exclude or deny the possibility of a biological *materies morbi*, but asserts that changes in the soil are of essential importance. The theory is essentially adopted by Creighton. After the discovery of the bacillus this doctrine lost popular credit and I think that most people would now hold that in the countries of indigenous cholera, contamination of the water supplies is the normal means of keeping the disease alive, while the outbreak of cholera in other countries is due to the arrival of patients or more often healthy carriers. Hence in prophylaxis most weight is put upon quarantine. There are various objections to that view; they are expounded with vigour, even with passion, in Sticker's treatise. In my opinion in order to reach if not the truth at least a clear appreciation of how we should seek truth, it is necessary to study cholera in places where it is endemic, but yet its manifestations are on a sufficiently small scale for the facts to be comprehended as a whole. On that account I think Flu's memoir, entitled "Epidemiological Studies of Cholera in Batavia, 1909-15," which appeared in the medical journal of the Dutch Indies,\* is very important. It is by no means the only paper written in Dutch which English epidemiologists should read—we have a good many vital statistical and epidemiological lessons to learn from our Dutch colleagues in the East.

Flu was not dealing with epidemics running into thousands of cases. His investigation begins in 1909 and he records 200 cases in September of that year, 350 in October, 210 in November, 130 in December. In 1910 the monthly incidence was 140 in January, then 105, 170, 150, 220, 310, the maximum of the year in June, then 225, 235, 160, 80, 32, 60. In 1911 there were few cases in the first three months, 42, 18, and 45, then a great maximum of 400 in April, 380, 160, 30, 50, 130, 80, 50, 15. In 1912 there were only units until August contributed 18 and September 240, the last three months 180, 60, 6.

In 1913 the numbers reached 150 in May, 169 in June, then 90, 148, 30, 70, 50, and none. In 1914 there were no cases at all until August, with 110, and then as many as 657 in October, falling to 50 and 30 in the following months. Important but not overwhelming prevalences, with maxima not all occurring

\* *Geneeskundig Tijdschrift voor Nederlandsch-Indië*, Deel 55, 1915, pp. 863-925.

at the same time of the year. Graph 2 shows the course of events.

Batavia is a city of at least 150,000 inhabitants (probably many more) and in close connection by sea with the rest of the Dutch possessions. The coolies and even the poor whites disregard the most ordinary rules of hygiene, faeces are deposited anywhere, there is no real system of sewage disposal. There are settling tanks for drinking water, but many really drink river water. Bathing-places are liable to gross contamination. No attempts are made to destroy the breeding-places of flies which in due season swarm around dwellings.

The general belief in Batavia has been that cholera is brought to an end when the rain sets in. It is, however, certain that cholera can and does prevail during the rainy season, although examples of the apparently favourable effect of rain can easily be given. Flu's graphs suggest that the first effect of rain may be to increase the number of cases of cholera, no doubt owing to the sweeping into the rivers of the polluted surface debris; it is only gradually, when the ground has been persistently soaked, that the drowning, as it were, of cholera takes place. During the dry season the ground becomes biologically inactive, after rain various forms of life spring into activity. Flu observed that the survival of cholera vibrios in the soil of compounds infected with cholera amounted to two, at most three, days in the west monsoon, the wet period, but had a mean of four and a maximum of six days in the east monsoon. This is of importance owing to the part played by flies. Also the better opportunities of flies to breed undisturbed in water-holes during the dry season (when these fill with rain naturally the broods are washed away) are very important. The breeding cycle of the fly is one factor of the latent period between the coming of heavy rains and the diminution of cholera.

Investigation of samples of water during a cholera period September–November 1913, all samples having been taken in the immediate vicinity of a hut within which a case of cholera had occurred within twenty-four hours, did not, however, show a very large proportion of infected waters; of seventy-two samples only five gave positive results. In river water vibrios die out rapidly: the presence of protozoa is an important factor of this.





There is no satisfactory evidence that cholera vibrios can survive saprophytically for any length of time either on the feet or in the guts of flies. We are therefore forced back to the conclusion that man is the reservoir of cholera infection, the gall bladder carrier of typhoid is probably paralleled in cholera. All this does not, however, satisfactorily explain the explosive character of the epidemics, and, indeed, Flu provides no adequate explanation. He does, indeed, argue that an epidemic is brought to an end by the increasing immunization of the population at risk not merely by passing through clinical attacks but by sub-clinical attacks. It is hard to believe that this can really be the explanation, because, as already pointed out, the total number of cases is very small in comparison with the exposed to risk. We should have to postulate an immense number of sub-clinical cases. Flu's own statistics of the percentage of cholera carriers amongst the contacts of those clinically ill—based upon three hundred and sixty-four contacts during the epidemic of 1914-15—was 8.29. If, therefore, carrying were the criterion, evidence of widespread sub-clinical infection is trivial. It seems then that the mystery of the explosiveness remains a mystery. The importance of Flu's study is in making it probable that in a land where conditions are favourable for dissemination, the existence in the community of human carriers is the means of keeping the disease alive. Flu does, indeed, advance some arguments for holding that massive anti-cholera inoculation may have some effect, but these are not very substantial.

There is, I think, strong evidence that anti-cholera prophylaxis has been, and may be again, of considerable value in saving life under conditions of acute exposure to risk—for instance under war conditions in the Near or Far East—no very convincing evidence that in this way the epidemiology of natural cholera can be modified.

As seems so often to be my fate I must end on a note of interrogation. Why did the Indian variety of cholera acquire a dispersive power a little more than a century ago? Why did it ravage Europe for more than a generation and then lose interest in us? Without going the whole way with Sticker I am prepared to go some distance and to doubt whether the decisions of national and international committees or the blockading of land or sea

frontiers have played a much more important rôle than the fly on the wheel. I cannot comfort myself very much with the notion of either epidemic constitutions or the germinal vitality of strains of micro-organisms. This tribute, however, should be paid to the *Manes* of John Brownlee and those who share his view. Our endemic cholera, the murderous diarrhoea of young children, has changed wonderfully in the present generation. We can no longer pick out a hot summer (when a hot summer occurs) as easily from the record of mortality of the young as from the reports of the Meteorological Office. Something has changed very greatly: perhaps we may call it the soil in which crowd illnesses of the particular type of which asiatic cholera is the most terrible example flourish. What that change is we do not know.

#### RECOMMENDATIONS FOR FURTHER STUDY

In addition to the classics and to the paper by Flu cited in the chapter, I must refer to Sticker's treatise (*Abhandlungen aus der Seuchengeschichte und Seuchenlehre*, II, Band, *Die Cholera*, Giessen, 1912). This is the best documented history of the subject I know, and some of it is very good reading. As a whole the book suffers from lack of form and a tendency to polemics which are not very interesting, although, perhaps, one ought to be interested in them.

### III

## TYPHUS

PROBABLY the great majority of readers have never seen a patient suffering from typhus; so far as the England of our generation is concerned, typhus is more exotic than plague. Between 1919 and 1931, 37 cases have been reported in England and Wales. In the last five of these years, 1927-1931, 6 only, in the last two none at all. In the last two years France has had 3 notified cases, Germany 2. Passing eastwards, the picture changes. In those two years Poland had 3,569 cases, Lithuania 730, the Soviet Socialist Republics 37,491. This last seems a large number, but is a trifling item in the total account of Russia since the war, which from 1919 to 1930 reached nearly 8,000,000.

We must go back nearly fifty years to reach a death-rate from typhus in England and Wales at or above the level of one in a hundred thousand. Fifty years ago the rate was 1·2 per 100,000 (328 deaths); sixty years ago it was 7·4 per 100,000 (1,762 deaths). The experience of Germany has been similar; in 1884 her rate was 0·5 per 100,000 (422 deaths). Scotland, rather less fortunate, did not fall below the 1 per 100,000 level until 1900; Ireland has only been consistently below that level since 1922.

In Asia, America, Africa, and Australia, typhus occurs. The territories for which more than a thousand cases were returned in 1931 were: In Africa, the Union of South Africa (1,663); in America, Mexico (1,445); in Asia, Corea (1,466), and Siberia (3,692). These figures are mere indications, the circumstances under which typhus occurs are not favourable to the compilation of accurate statistics; countries which collect no statistics at all are likely to be countries in which typhus prevails.

In studying it we must distinguish between a purely intellectual and a practical knowledge of its nature and aetiology. Our purely intellectual apprehension is still incomplete. It is not possible to isolate from the voluminous literature of fevers in pre-Renaissance medicine any clear-cut description of what we now call typhus. Fracastori in 1546 first gave such an account in a description of epidemics in Italy in 1505 and 1528. He described the ex-

anthem, which, he said, the common people likened to flea bites, and expressed the opinion that "this fever is contagious, not rapidly, not *per fomites*, not at a distance, but only through contact with the patient." He gave what later clinicians have found to be an adequate account of the signs and symptoms of the illness. This description was not greatly improved upon until the time of Huxham, whose differentiation of the malignant from the slow nervous fever may stand for a fair distinction of typhus from typhoid. Professional opinion differentiated what we call typhus from the pestilential fever we now recognize as bubonic or pneumonic plague, and thought of it as involving a corruption, a fundamental deterioration, of one of the humours; hence the usage of such terms as putrid, malignant, etc., fever. These views prevailed down to the nineteenth century, and, after the humoral pathology had become obsolete, there was still a certain doubt as to whether typhus were *ab initio* a biological process repeating itself in perpetual succession from an authentic germ. In that once famous—and still readable—"shocker" by Wilkie Collins, *The Woman in White*, when the heroine falls ill of a fever, the doctor is asked whether it has turned or is likely to turn into an infectious fever. In due course it does become infectious. That incident is a reflection of the semi-popular view that what we should now perhaps call typhoid might mutate into typhus, the former not being and the latter being a contagious illness. Even in the student days of men still living, the mechanism of conveyance from the sick to the healthy was unknown; indeed, it is only within the present generation that the conveyance by body lice has been universally accepted and demonstrated in a way acceptable to all. Precisely what is conveyed is still a matter of dispute among the adepts. Even now our intellectual grasp of the whole detail is incomplete.

On the other hand, our practical knowledge of the way in which typhus is generated and of how it may be prevented has been complete enough since the time of Queen Elizabeth at least.

Although the venereal diseases have usually been regarded by moralists as the exemplar of divine punishment of human wickedness, the attribution is unsound. Epidemic typhus is a much more imposing monument of man's wickedness, of his *inexcusable*

wickedness, and its punishment. Prophylaxis of venereal disease is made difficult by the inhibitions and constraints of psychological factors which are quite beyond the control of conscious thought. Epidemic typhus does not excite these emotions, and, certainly since the sixteenth century, men have known quite well the essential aetiology of crowd typhus. There has not been a time when the connection between what we call typhus (it has been called putrid fever, gaol fever, camp fever, and many other names) and social misery was not clearly recognized. Huxham two hundred years ago knew that putrid fever was *really*—i.e. academically—due to a “too moist and thick constitution of the atmosphere,” but he also knew that those attacked were mostly “very weakly, or have their spirits greatly broken by trouble or use a crude, unwholesome diet, as is the case commonly in prisons.” The city chamberlain of Exeter, one hundred and fifty years before Huxham’s time, realized that just as clearly. He correctly traced an epidemic of typhus which slew some important people to the appearance before the Queen’s Lords Justices of Assize of certain “Portingals” who had been taken on the high seas by one Bernard Drake—perhaps a relation of a more famous buccaneer. These prisoners of war had tasted our old English hospitality—which was no worse than any other nation’s. They had been taken to the gaol and there “cast into the deep pit and stinking dungeon. These men had been before a long time at the seas and had no change of apparel nor laine in bed and now lieing upon the ground without succour or reliefe were soon infected and all for the most part were sick and some of them died and some one of them was distracted and this sickness very soon after dispersed itself among all the residue of the prisoners in the gaole.” The production of these prisoners, the survivors of them, in court, “Moved manie a man’s heart to behold and look upon; but none pitied them more than the lords justices themselves.” One of the Lords Justices was vouchsafed time to give practical effect to his sympathy. But the other, and many curious sightseers, although each man departed (as he thought) “in as good health as he came thither,” were fatally seized by an illness “which resteth for the most part about fourteen days and upwards by a secret infection before it breaks into his force and violence.”

It is needless to multiply examples. As there is no evidence that during the next two centuries following the martyrdom of the "Portingals" in Exeter gaol anything effective was done to better the condition of prisoners, it is not surprising that similar incidents recurred. One of the last of the Black Assizes was in 1750 at the Old Bailey, and its description by Pringle is much the same as, although less picturesque than, that of Holker. A point of interest in Pringle's account is the way in which persons in court sitting at particular points were picked out. "It was remarkable that the Lord Chief Justice and the Recorder, who sat on the Lord Mayor's right, escaped, while he himself, with the rest of the bench, on his left, were seized with the infection; that the Middlesex jury, on the left side of the court, lost many whilst the London jury opposite to them received no harm; and that of the whole multitude, but one or two, or at most a small number of those who were on the Lord Mayor's right hand, were taken ill."

That was as explicable in terms of some effluvium, some capricious blast of bad air, as in those of louse migration, so naturally Pringle—who knew nothing of the significance of so common a guest as the louse—explained it in those terms. He had what seemed confirmatory evidence in the fact that of a bevy of carpenters employed on the ventilator of Newgate, seven out of eleven died of gaol fever. One of the victims was an apprentice who had been forced by the men to go down into the shaft of the great ventilator to recover a wig somebody had thrown in.

Cases illustrating typhus as the concomitant of social wickedness on a domestic scale could be multiplied indefinitely. War, being social wickedness on the largest scale, has naturally furnished examples which are statistically more impressive. No large-scale European war has failed to provide examples. Probably the seventeenth-century war of thirty years provided the largest display of typhus which has yet occurred. In Württemberg the population was reduced from 400,000 to 48,000. A contemporary wrote: "One may wander ten miles and see no living man or beast, save perchance an old man or a child or two old women. In all the villages the huts are full of corpses, man and wife, children, apprentices, sheep and oxen, slain by disease and hunger, eaten of wolves and foxes, crows and ravens, for there was none

to bury them." The Napoleonic wars come, perhaps, next. The late war, however, secured a fairly adequate harvest. In Serbia between 100,000 and 150,000 persons out of a population of perhaps 3,000,000 are said to have lost their lives, and in the prison camps of Germany and Russia very respectable epidemics occurred. A sufficiently dramatic and brief illustration of war typhus is the story of 1812 as summarized by Haeser.

Napoleon's grand army consisted of between 500,000 and 600,000 men, less than half of whom were French. The Sixth Army Corps, of a strength of 28,000, consisted of Bavarians, the Seventh, 19,000 strong, was Saxon, the Eighth, 19,000 strong, was Westphalian. Macdonald's Tenth Corps was made up of Prussians, Bavarians, Westphalians, and Poles. When concentrated on the line of the Weichsel in April 1812 there was little sickness. During the advance through Poland respiratory affections began to be noticed, but not typhus. The Niemen was crossed on June 23rd and admissions to hospital at Vilna reached 5,000. After leaving Vilna rain set in, and the commissariat arrangements, faulty from the start, began to show signs of breaking down. Diarrhoea and dysentery now began to be noticed and by July 25th, when Ostrow was reached, the sick numbered 80,000. Witbsk was taken on July 28th and its hospitals crammed with sick and wounded. From this point typhus was predominant; the epidemic culminated in the early autumn. The Third Corps, for instance, had only 12,000 effectives out of 43,000 when Moscow was reached on September 14th.

The beginning of the retreat on October 18th found the army reduced to 80,000 effectives. Smolensk was reached on November 8th and from 15,000 to 20,000 sick were left in the town. Typhus and dysentery, together with losses in the action on the Beresina, accounted for 40,000 more, and only some 20,000 recrossed the Niemen on December 13th. The remnant which reached Vilna was ravaged by typhus, and of 30,000 prisoners in Russian hands 25,000 are said to have died of typhus. The few who survived to retreat over the Weichsel are said to have shown an improvement coinciding with the provision of adequate hospital accommodation.

Experiences either in Serbia or in the prison camps of our own time add nothing significant to this story. A good typical

account is that by Major P. C. T. Davy and Captain A. J. Brown\* of Gardeleben. There some 2,000 cases occurred amongst 12,000 prisoners, with a fatality-rate of 15 per cent. Underfeeding and gross overcrowding played here the same part as in 1812.

The accounts of domestic typhus, like those of war or prison typhus, resemble one another closely. I choose as quite typical and common-place Dr. James Johnstone's account of the origin of the Malignant Epidemical Fever of 1756 in the town of Kidderminster. He first tells us how in 1755 at the time when "happened that dreadful earthquake which laid Lisbon in ruins, which shook the whole Atlantic Ocean," odd geological events occurred, and the "waters of Severn and some fish ponds in our neighbourhood, were tossed and agitated in a manner very extraordinary to the spectators." These events are, of course, theoretically relevant, if we believe in Sydenham's constitutions, as, perhaps, Dr. Johnstone did. We pass into the next year and are introduced to more directly relevant phenomena: the fruit blossom was destroyed by an untimely spring frost, the "seasonable maturation and gathering in of the corn crops, was obstructed by the long heavy rains—the dearth of corn increased very fast—and a dangerous malignant, contagious fever, which first appeared in April, was now become very epidemical." This fever "prevailed chiefly in poor families, where numbers were lodged in mean houses, not always clean but sordid and damp. It seemed to affect such poor families most, where there was reason to think a sufficiency of the necessities of life, on account of the dearth, had for some time been scantily supplied."

This is a story which has been told hundreds of times. Creighton's account of typhus in England in the first quarter of the nineteenth century is classical. One point in it may be emphasized, viz. the comparative immunity of England from "fevers" of which typhus was the most important during the period of artificial prosperity between 1803 and 1815. Knowing what we now know of the biology of typhus as an individual process, we shall not, of course, attribute typhus to starvation alone. Indeed, long ago, instances of famished populations in which typhus did not occur, e.g. in some islands off the Irish coast during the great famine of 1846-7, were recorded. But it usually happens that a starving population

\* *British Medical Journal*, November 20, 1915.

is also an overcrowded population, that in the cold weather ill-fed people huddle together for warmth. Even then, if the *materies morbi* is not widely disseminated through the population, an epidemic may not be generated. Our great-great-grandparents of the beginning of the nineteenth century in England were no doubt very lousy, but not more lousy than the troops on the Western Front in 1917. But typhus never appeared on the Western Front, while after the false prosperity of 1803-15 it became virulent in London. The difference was that the English ports, such as Liverpool and London, were always receiving immigrants from Ireland fleeing from a destitution even worse than that of English town slums and bringing the *materies morbi* with them. Had Russian troops been brigaded with the English on the Western Front, then even the adequate rationing might not have sufficed to prevent at least sporadic typhus.

From the point of view of preventive medicine, typhus is, in theory, the most controllable of diseases. In an adequately fed and housed population it simply cannot occur as an epidemic disease—in theory; our ancestors who did so little to prevent it, may not have been harder hearted than we are. They did not, however, know how to prevent wars on a large scale or how to secure an adequate distribution and use of food, soap, and water. No doubt we do. If we do, and if we use our knowledge, the interest of typhus will become purely archaeological. At present it is of more than archaeological interest in many parts of the world.

#### RECOMMENDATIONS FOR FURTHER STUDY

The writers I have so often cited and recommended, viz. Creighton, Hirsch and Haeser, will again be the student's best guides. For the war experience, cf. *Official History of the War. Medical Services. Diseases of the War*, Vol. I, p. 133.

## IV

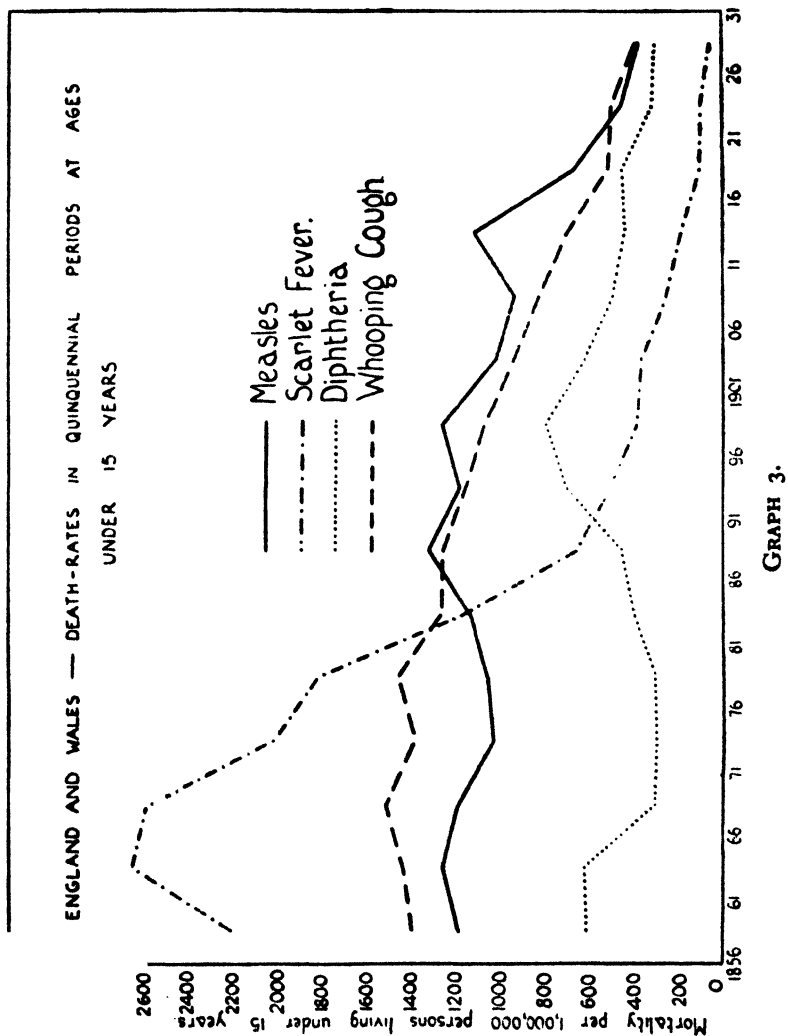
### MEASLES

SANITARIANS and laboratory workers take much more interest in diphtheria or even scarlet fever than in measles. Few people can take the measles of other people or other people's children quite seriously. One reason is the ubiquity of measles. Most of us remember that although the second wave of the pandemic of influenza in 1918 killed more people in England and Wales within a few weeks than any outbreak of acute crowd-sickness since the Black Death, there was no panic at all in cities of Western Europe. A rumour of plague or the reality of "spotted fever" has always excited quite definite fear. No doubt preoccupation with the horrors of war was an important factor of psychological indifference; another was the universality of the disease. Influenza slew, indeed, its thousands, but it prostrated its millions; one does not readily fear what is so familiar, and, to most, so little deadly. Thus it is with measles. Although the number of deaths ascribed to measles is on the average a good deal larger than the total debited to diphtheria (see Graph 3) the fatality-rate is much lower. We are afraid of diphtheria, but not of measles.

To the historical or statistical epidemiologist, however, measles is an interesting illness, and perhaps the time has come when the practical sanitarian may be given an opportunity of mitigating the havoc it makes.

It is probable that the *Hasbah* of the Arabist writers, translated into mediaeval Latin *Morbilli*, covered more than our measles, but the clinical account does warrant us in holding that "genuine" measles was a large constituent. It may perhaps be taken as evidence of a change of type that "Rhazes" (Abu Becr Mohammed Ibn Zacariya ar-Razi) said that "the measles are more to be dreaded than the smallpox except in the eye" (Greenhill's translation, p. 92). From the time of Sydenham measles as a "clinical entity" has certainly had very much the connotation it now has, and, with the aid of the Bills of Mortality, and for the last ninety years the national statistics, its course can be followed with reasonable certainty. To glean after Charles Creighton is not a

remunerative task and the reader need not look to me for new light on the period he covered. It is certain that measles was



seriously epidemic in London in 1674 and that throughout the eighteenth century pretty heavy toll was taken of young lives. But it does not seem that measles as a crowd-disease of childhood was a serious competitor of smallpox before the beginning of the

nineteenth century. The epidemic of measles in 1807-8 was, in Creighton's words, "a great and clearly defined event in British epidemiology, the first of a series of epidemics in which that disease established not only its equality with smallpox as a cause of infantile deaths but even its supremacy over the latter." A few years later Robert Watt in his famous study of the relative mortality of the principal diseases of children, concluded that measles was replacing smallpox and drew a rather pessimistic moral which may be summarized in the adage that what is gained on the swings is lost on the roundabouts.

Watt showed that, notwithstanding an enormous diminution in the proportional mortality of smallpox between 1783 and 1812 in Glasgow, the ratio of deaths under ten to total deaths had actually increased. He further showed that the relative mortality of measles had increased as that of smallpox decreased: thus the latter fell from 19·55 per cent in the first period of six years to 3·90 per cent in the last. The former on the other hand increased from 0·93 to 10·76. He wrote: "The great increase of deaths between two and ten years of age is very remarkable. In the first period they amounted to no more than 14·08 per cent; in the last period they come little short of 20 per cent. Are we to expect a continuation of this increase of deaths from ten to fifteen, generally a very critical period of life, and in the ages from fifteen to twenty? As matters now stand, we have gained under two; we have lost between two and five, and also between five and ten. At ten we stand nearly on the original level, but if we are to lose between ten and twenty it shows how truly abortive all our schemes have been. We may, it seems, by the permission of Divine Providence, deprive Death of some of his apparently most efficient means, but deprived of these, new means are discovered or the old improved."\* Fifty-four years later, in the Registrar-General's Annual Report for 1867, Farr discussed this lugubrious conclusion. As Watt was using not death-rates but proportional mortalities, his findings were really compatible with an improvement of mortality-rates; but Farr showed that in Glasgow, although mortality from smallpox had declined still further by the middle of the nineteenth century, the gross rate

\* R. Watt, *Treatise on the History, etc., of Chin Cough*, Glasgow, 1813, pp. 380-1.

of mortality on children in Glasgow had, if anything, grown worse. At the time Farr wrote, scarlet fever was a much larger cause of mortality in Glasgow than measles. In 1855-9 the respective death-rates per million were 1,301 and 901. In 1921-5 the death-rate from scarlet fever was 64 per 1,000,000, that from measles 476. Another half-century's experience, while not justifying Watt's pessimism in the absolute way he stated it, has brought to measles, relatively not only to smallpox but to the scarlet fever (and, indeed, to the diphtheria) of Farr's day, an immensely increased importance.

A striking feature of its secular history lends measles a particular fascination, viz. its periodicity. Measles seems to recur in epidemic form at intervals which in any one place are roughly constant for long periods of time. In London, for instance, epidemics of measles tend to recur in alternate years. Table 23, page 184, illustrates this feature.

It will be seen that there is not a large outbreak every alternate year, that exceptions to the rule occur, but that it is *roughly* true that in London epidemics have a biennial periodicity. We shall see later on how far that statement must be modified to make it accurate.

Naturally epidemiologists have been tempted to explain this phenomenon. Before discussing some explanations tendered, the postulates on which they rest must be examined. The first is that all children are born susceptible to measles and that a single attack confers lifelong immunity. It seemed well established that in urbanized communities only a small percentage of adults had not had measles. Brownlee for instance found that of 12,000 cases of measles at the Belvidere Hospital (Glasgow), 1885-1902, only 71 were of persons over thirty, and these were almost without exception persons born in the country who had not been exposed to infection in childhood. We shall find, however, that exposure to measles infection may confer some degree of immunity without the production of clinical illness. This has been made probable by the researches of Stocks.

Another postulate assumed in earlier explanations of the periodicity of measles is that the time during which a sick person is capable of infecting others is very short, that in this respect measles contrasts strongly with diphtheria.

This opinion is mainly based on clinical experience not easily presented in a statistical way, but such statistical data as we have

TABLE 23

LONDON: ANNUAL DEATH-RATES PER 1,000,000 FROM MEASLES, 1852-1901

Period	Death-rate	Period	Death-rate
1838-40 (3 years)	695	1871	437
1841-50	623	1872	505
1851-60	530	1873	637
1861-70	576	1874	490
1871-80	510	1875	404
1881-90	636	1876	485
1891-1900	583	1877	664
		1878	411
		1879	667
		1880	402
		1881	663
1852	246	1882	605
1853	398	1883	626
1854	563	1884	575
1855	345	1885	731
1856	569	1886	519
1857	509	1887	716
1858	884	1888	590
1859	488	1889	558
1860	752	1890	773
1861	377	1891	428
1862	816	1892	798
1863	562	1893	383
1864	942	1894	757
1865	431	1895	614
1866	730	1896	826
1867	370	1897	429
1868	625	1898	687
1869	458	1899	475
1870	450	1900	432
		1901	433

are consistent with its truth. A digression on the statistical measure of infectiousness may help to make this clear. Without any quantitative measure in our minds, we shall agree that if when a person suffering from a supposedly infectious disease is brought

into contact with, say, five susceptible persons, and all five go down with the disease, and if the observation is made a great many times on such groups, the result emerging that almost always 100 per cent of the susceptibles are attacked, then the disease is highly infectious. If in another disease similar observations lead to an attack-rate of only 25 per cent, we shall conclude that the second disease is less infectious. Of course this contention is not formally logical. We might have attack-rates of 100 per cent and of 25 per cent without any infection from person to person at all. If, for instance, all the members of the group of five had drunk the same typhoid-infected water as the original patient, we might reach 100 per cent of cases, and, according to the proportional distribution of water drinkers, we might reach 25 per cent, 50 per cent, or any other distribution of "secondary" cases. We could differentiate broadly between distributions of the latter and the former type by saying that in the latter type we should expect some conformity with a pure chance distribution of events. If, for instance, the individual chance of drawing a prize in a lottery were one in ten and all members of families of five persons each held tickets, then the percentages of families of five, all of whose members drew winners, four of whose members drew winners, etc., would be the six successive terms of the binomial  $(1/10 + 9/10)^5$  each multiplied by 100.

Such a distribution is not in the least like that of measles in families. For instance, during the epidemic of measles in St. Pancras in 1926 there were observed two hundred and twenty-eight families each containing, in addition to the child who first sickened, three other children under ten years. The following figures give the experience of these groups observed from four days after the appearance of the rash in the first case until one month after the onset of the last case in the group.

No cases	..	..	..	..	..	..	84
1 case	..	..	..	..	..	..	60
2 cases	..	..	..	..	..	..	57
3 cases	..	..	..	..	..	..	27

Now suppose we treat this on the lines of a lottery, determine the chance of winning a prize—the prize being to have measles—

by the ratio of children who did suffer from measles to the children exposed to risk, as recorded in the whole of the data, and then compute the binomial—the exponent of which will be three—we reach the following figures:

No cases	..	..	..	..	..	..	76.2
1 case	..	..	..	..	..	..	100.9
2 cases	..	..	..	..	..	..	44.4
3 cases	..	..	..	..	..	..	6.5

Evidently the hypothesis is wildly wrong. The distribution of secondary cases of measles is not in the least like that of lottery prizes.

Now let us suppose that all the cases after the first are generated by personal infection. If we adopt the postulate that a patient is only infective for a very short time, the binomial arithmetic will still be serviceable, but its method of application will be quite different. Let us suppose that the first patient has a certain power of infecting his contacts—he is, perhaps, bombarding them with infective droplets; we may say that he is distributing lottery tickets of which a certain proportion are winners. But he soon exhausts his supply. If he has infected nobody, then there will be no more cases; if, however, he has infected, say, one person, then that person will in his turn distribute tickets to the group, now reduced by one, who are liable to infection. On this hypothesis we can reach a final total of, say, three secondary cases in a group of three contacts in several different ways. Let the proportion of infective shots or “winners” be  $p$ ; then, on the old hypothesis, the cube of  $p$ ,  $p^3$  would measure the proportion of three, all members of which were infected.

On the present hypothesis we could reach three infected out of three in the following ways:

(1) Three cases from the first case, and, of course, no more. Measured by  $p^3$ .

(2) Two cases from the first exposure and then one case. The probability of the former event is  $3p^2q$  (where  $q = 1 - p$ ), of the latter  $p$ , because there is but one person at risk so the binomial  $(p + q)$  has unity for its exponent. Combined probability,  $3p^3q$ .

(3) One case from the first case and two from the second.

The respective probabilities are  $3pq^2$  and  $p^3$ . The combined probability  $3p^3q^2$ .

(4) One case from the first case, one from the second exposure, and one from the third; the several probabilities are  $3pq^2$ ,  $2pq$ , and  $p$ , their product  $6p^3q^3$ .

In this way we can work out the whole number of ways of generating 3, 2, 1, and 0 secondary cases, and, from the data, a suitable value of  $p$  may be deduced. The result in the example taken is that, putting  $p = 0.26716$ , we have:

No cases	..	..	..	..	..	..	89 7
1 case	..	..	..	..	..	..	52.7
2 cases	..	..	..	..	..	..	54.4
3 cases	..	..	..	..	..	..	31.2

Now the agreement between observation and expectation is reasonable. The distribution is in fact very much what we should expect if each person with measles made an instantaneous distribution among the susceptibles of lottery tickets of which rather more than a quarter were winners.

Other *pièces justificatives* and a detailed description of the method of computation will be found in my paper on the subject.\* I think the results are a fairly adequate justification of the hypothesis that measles is infectious for only a very short time.

Upon the hypothesis of a very short infective period and the further common-sense hypothesis that the number of fresh cases generated by existing cases will depend in some way upon the proportion of susceptibles in the population, Sir William Hamer showed how a periodicity similar to that of measles might arise. When we are dealing with an illness only conveyed from person to person, it is clear that if at any instant of time each existing case generates just one new case, the incidence of the disease will be constant; if each existing case generates more than one fresh case the incidence will increase; if it generates on the average less than one case the incidence-rate will decrease.

When, as in measles, the incidence rises and falls in waves, then there are two points, viz. the crest and the trough of the wave, where for a moment the incidence-rate is steady, one case generates one new case. Just past the crest in the next instant one case

\* *Journal of Hygiene*, Vol. XXXI, 1931, pp. 336-51.

generates less than one. Just past the trough in the next instant one case generates more than one. Hamer showed that on the supposition that some 2,500 susceptible children were added to the population of London every week, then measles would pass through a cycle from crest to crest of about seventy-eight weeks. The crest of the wave would be when about 6,400 cases occurred per week and the susceptibles numbered about 150,000; then the new weekly cases would decline, but would still outnumber the new additions, so that the susceptibles would continue to decrease for about fifteen weeks, when they would amount to about 120,000. From that point, as the new cases continued to decline while 2,500 susceptibles continued to be added weekly, the susceptibles would increase until by the thirty-ninth week they again amounted to 150,000. That critical value having been reached, the weekly addition of cases would increase, at first not fast enough to overtake the addition of susceptibles, which would reach a maximum of 180,000; but, as the increase continued, the balance would be reduced until by the end of the seventy-eighth week one had again 150,000 susceptibles and a fall began, the cycle repeating itself. In other words 150,000 susceptibles represented a critical value; when approached by an *increasing* attack-rate the increase passed through a stationary point into a decrease; when approached by a *decreasing* rate the decrease passed through a stationary point into an increase. Hamer's work was published a quarter of a century ago. More recently that brilliant mathematical statistician, the late H. E. Soper, followed the trail blazed by Hamer, using a characteristically beautiful method, the essence of which I shall try to explain in non-mathematical terms.

The hypothesis we are discussing requires us to believe that the number of cases generated in any short interval of time is proportional to the number of susceptible people then present in the community. Let us say that number is  $x$ , and that when measles is endemic, one new case replacing one pre-existent case, the susceptibles are the fixed number  $m$ . If instead of  $m$  we have  $x$ , it follows that instead of one new case for each old case we shall have  $x/m$  new cases for each old case. But we may think of  $m$  as compounded of two factors, viz. the actual number of susceptibles added per time-interval, say  $a$  and some factor we may call  $s$ , which will measure the conditions—e.g. of seclusion or

commingling—of the particular crowd we are studying. We may write then  $m = sa$ . We are brought to this relation :

$$\frac{x}{sa}$$

The number of cases generated in an interval divided by the number of cases generated in the previous interval must be equal to the number of susceptibles present divided by  $s$  times the accessions per interval.

Soper found that this expression led to periodic curves of Hamer's type. But the particular type of biennial epidemics (the maxima in alternate years, but not separated by two years but more nearly eighteen months, a winter epidemic in one year followed by a summer epidemic in the next year but one) which characterized London is not universal. One sometimes has annual epidemics modified by seasonal exacerbations. Soper accordingly modified the right-hand side of the equation just described, introducing a periodic factor (i.e. a term which passes through a cycle of values as the independent variable increases or decreases steadily) and studied the detailed history of measles in Glasgow. The extent to which the hypothesis as formulated by Soper conforms to reality may be best judged from the following considerations. A test of the adequacy of such a hypothesis is its power to describe the observations and to permit one, from knowledge of an antecedent in the time-series, to predict a consequent. Soper applied that test to the Glasgow data of 1905-16 with the following result. If one merely predicted that in the next fortnight in a series there would be precisely as many cases as in the current fortnight, i.e. that one had a steady state, then the average error of the prediction was 21 per cent. If one used the method just described the error was reduced to 10.5 per cent. This method, then, which postulates that the ebb and flow of measles is a function of the ebb and flow of susceptibles modified by seasonal change, may be said, in Soper's words, "to give half the picture."

When we recall that the data themselves are not very accurate and that in real life a myriad of small disturbing factors *must* have play, it seems reasonable to conclude that Hamer and Soper have found not the whole truth but aetiological factors of real importance.

Let us now examine a wholly different way of studying and interpreting the phenomenon of periodicity. Periodicity, as Farr said of geometrical progression, is, like Ariosto's Ippogrif, a "difficult horse to ride, and sometimes lands people in strange conclusions." Economists who have not sufficiently taken to heart the content of Fourier's famous theorem have sometimes illustrated this. One can always translate secular arithmetical series into harmonics, but what one really needs is some criterion that the deduced periodicities have an objective meaning. It may happen that a long series of records is available and the task is to ascertain whether objective periodicities are lying concealed. To reveal these is the object of what is called periodogram analysis. This is a difficult and delicate art, but an intimation of its nature can be given without any mathematics. Suppose we had a strictly periodic series of numbers, say 1, 2, 3, 4, 5; 1, 2, 3, 4, 5; 1, 2, 3, 4, 5, and so on *ad infinitum*. Evidently if we wrote down these numbers in rows of five, thus:

1	2	3	4	5
1	2	3	4	5
1	2	3	4	5
1	2	3	4	5
1	2	3	4	5

and added up each column, then as all the 1's are in the same column and all the 5's in the same column, the difference between the smallest and the largest sum would be as great as these numbers would admit of. But if we made rows of four we should have:

1	2	3	4
5	1	2	3
4	5	1	2
3	4	5	1
2	3	4	5

Now all the columns have the same sums. The same thing will happen if we add up in rows of 2, 3, 6, 7, 8, or 9. When we come to rows of 10, we shall have two columns of 1's and two columns of 5's.

This suggests that when one is dealing with a long series of numbers which may depend upon periodic factors, the lengths of these periods could be determined by systematically adding up in column rows of different lengths. That is the principle of

the method of searching data for concealed periodicity. It is hardly necessary to say that in actual practice there are many difficulties to overcome. The first epidemiologist to apply this method to the study of crowd-diseases was the late John Brownlee, and he applied it with particular assiduity to the data of measles. London naturally provided the longest run of figures, since data of a sort are available from 1703 and reasonably accurate data since 1838. Brownlee found, using the method the principle of which has just been described, that between 1838 and 1913 periods of 87, 89½, 97, 105, 106, 109½, and 114 weeks were revealed; of these the 97 weeks' period was much the most important. "The question of the permanence of these periods," wrote Brownlee, "immediately arises. With regard to that of the 97 weeks this admits of no doubt, but the others are not so definitely in evidence. . . . The conclusion therefore seems to follow that in London there are a number of epidemics of measles with different periods, these epidemics assuming greater or less importance. Of these the chief is the epidemic of 97 weeks' period which remains the dominant epidemic from 1840 to the present day" (this was written in 1919). Brownlee also studied the intra-local distribution in London between 1890 and 1915, and came to the conclusion that the epidemic with a period of 87 weeks only existed south of the Thames, while that with a period of 97 weeks was present in all London districts. Brownlee investigated in similar fashion the data of many other cities. In Glasgow, for instance, he revealed periods of 98 and 109 weeks. In Sheffield he found a main period of 96 weeks and a less important period of 104 weeks.

In Brownlee's view these periods reflected the life cycles of different strains of organisms and that hypothesis does not appeal to me. It seems to me a mere restatement in rather fantastic language of the arithmetical results. I see no reason to doubt the reality of Brownlee's findings—although there might be some difference of opinion among those more skilled than I am in the difficult mathematical-statistical analysis required as to the sufficiency of some of Brownlee's tests, it is *very* unlikely that the periods he characterized were mere random fluctuations. At present, however, the results must remain a little apart from the course of everyday investigation. We cannot yet interpret them in a way congruent with our general knowledge. The time will

surely come when they will fit in. No thorough and accurate study, such as pre-eminently Brownlee's was, is ever wasted.

Provisionally, then, it is best to be superficial, to think of the aetiology of periodicity in terms rather of ebbing and flowing susceptibles than of some profounder underlying biological factor. In another generation that may not be the path of prudence, but in epidemiology, as in other practical studies, it is best not to pretend we understand something we do not understand.

I pass now from these wider perspectives to a narrower scrutiny. The researches we have considered are concerned with massed figures, those to which I now turn are based on the analysis of detailed information. Dr. Percy Stocks with the help of Miss Mary N. Karn has made an intensive study of the history of measles in the Metropolitan borough of St. Pancras from 1916 to 1928. The Public Health Department of St. Pancras placed at the disposal of the investigators the record cards of 10,710 cases of measles, and this ample material made the modification of the hypotheses upon which some of the previous conclusions were based imperative.

First of all a very careful actuarial study of the population made it probable that an appreciable proportion of the inhabitants did not have measles at all. Stocks and Karn, indeed, concluded that as many as 30 per cent of the children born had the expectation of going through life without ever being *notified* as suffering from measles. No doubt some of these did actually pass through an attack, but statistical analysis led to the result that if immunity to measles could *only* be acquired by passing through a definite clinical attack, then the changes in the proportion of non-immunes at different ages seemed insufficient to account for the secular variation.

This suggested that a latent immunity, consequent upon what might be called a sub-clinical infection, played a part. This surmise was tested by following up the children who escaped measles in a house where a case had occurred, and by comparing their reaction in another epidemic after different intervals of time with that of control groups of children not previously exposed. It appeared that the exposed unattacked children of one period had a lower attack-rate when exposed again a few months later, but that the supranormal resistance gradually declined and at the

end of perhaps rather more than three years had passed away. In children who had passed through an epidemic without clinical attacks, but had not been house contacts of children with clinical disease, the acquired immunity declined faster and might be supposed to have passed away at the end of rather more than two years. Hence the hypothesis of periodicity determined by the ebb and flow of immunes must be extended to cover the fates of children not attacked but rendered temporarily immune.

The suggestion is that most of the children under ten who have not been actually attacked do become temporarily immune, and that more than half of these retain their immunity through a winter, but that most are susceptible after a further year. Stocks and Karn also studied the apparent infectiousness of measles at different phases of the epidemic cycle by computing the frequency with which second cases in children under ten occurred in the same house as a primary case, with an interval of ten to thirteen days between the appearance of the rash in the first and second cases. The result led them to conclude that, (1) the apparent infectiousness was five or six times as great at the start of a major epidemic as in inter-epidemic times, (2) it declined during the epidemic, and (3) rose before the epidemic, first gradually then steeply. All changes, save sudden fluctuations, might, they thought, be explained in terms of varying immunity (in the more general sense just explained). Some slight evidence of a relation between increased infectiousness and certain meteorological factors, especially atmospheric pressure, was discovered.

In the investigators' words: "A satisfactory explanation of most of the epidemiological phenomena of measles is thus provided by the concept of an active plus latent immunization of the child population on the one hand, and changes in facility of transmission of the virus by droplet infection from cases or carriers to other persons coming in contact with them on the other. If we suppose that this facility can be suddenly increased two- or threefold by favourable combinations of seasonal and atmospheric conditions, most of the phenomena can be explained without recourse to such vague generalizations as 'biological modifications' of the virus, though a few, such as certain cyclical changes in the seasonal incidence of measles epidemics, still remain unsolved."<sup>\*</sup>

\* Stocks and Karn, *Annals of Eugenics*, Vol. III, 1928, p. 398.

I am not enamoured of Brownlee's certainly vague goddess, but perhaps Brownlee, had he lived to read the last passage quoted, might have put his head a little on one side and smiling characteristically have remarked that the unexplained cyclical changes of the last sentence were just those *he* held to be most interesting.

J. L. Halliday's researches are contained in a report made to the Medical Research Council (Report No. 120 of the Special Report Series, published in 1928) and his contribution to the discussion of Soper's paper read to the Royal Statistical Society.\* The former is a demonstration of the prejudicial effects of tenement housing of the kind predominant in some areas of Glasgow in generating measles at an earlier age than when the housing conditions are better.

The official figures which, in Halliday's view, understate the case show that in the tenement areas of Glasgow and Aberdeen 58 per cent of the cases occur at ages under five years, in the non-tenement areas of Birmingham and Renfrewshire only 45 per cent. The importance of this is that the fatality of measles at ages under two years is from 10 to 20 times, at ages 2-3, 8 to 11 times, at ages 3-4,  $3\frac{1}{2}$  to  $4\frac{1}{2}$  times, and at ages 4-5,  $1\frac{1}{2}$  to 2 times as great as in the age group 5-10.

Brownlee some years ago (*British Medical Journal*, April 17, 1920) emphasized the importance of seeking to postpone the age of attack. He was disposed to attribute more importance as *primary* foci to the schools than the homes (of course this in no way impugns the importance of the home as a means of dissemination) and advised the following routine. Each school should maintain a register, and when a child of five was admitted a note should be made whether the child were the eldest, intermediate, or youngest of the family. When measles broke out in the class the register was to be consulted, and if the child were not the youngest member of the family, particularly if there were brothers or sisters between the ages of six months and three years, the child should, if practicable, be boarded out, with relations, from the seventh day of exposure until risk of clinical attack had passed.

How far the method is practicable I have not to discuss, but

\* *Journal of the Royal Statistical Society*, Vol. XCII, 1929, pp. 67-69.

it may be said that the postponement of the age of attack is surely the most important part of applied epidemiology in measles. Because it has long been so recognized is not a good reason for ignoring it.

Returning to Halliday's investigations, his observation of Glasgow led him to attach particular importance to a seasonal refractory period in May. He was inclined to account for the periodicity of measles on the following lines. In a large city such as Glasgow an epidemic took time to cover the whole field. When such an epidemic began in September some twenty-four weeks were required for it to cover all thirty-seven sections of the city. Were its origin postponed to January-March there was not time to cover the whole city before the refractory period began. Now on the former hypothesis the whole city would be covered, a considerable amount of immunity produced, and there would be no recurrence of epidemic dimensions for two years. If, however, the epidemic began late, then, as explained, the whole city was not covered and another epidemic might be generated the following year. In smaller communities, the epidemic would spread throughout and the periodicity would tend to be biennial. It will be seen that in a general way Halliday's doctrine is similar to that of Stocks and Karn; indeed, in his special report Halliday noted that all the exposed to risk in tenement houses were not attacked by clinical measles and postulated the development or a partial and temporary immunity.

Briefly, to sum up, we may, I think, hold that in the rise and fall of measles as a crowd sickness varying states of immunity largely determine the course. We must admit that this is not the whole explanation and that Brownlee revealed cycles which it is very hard indeed to understand. Such statistical investigations as have been made throw no real light upon changes of clinical type in an urban community, but it may be that in the future Brownlee's quite vague, and, to most of us, unhelpful interpretation of what he found will be transmuted into a powerful working hypothesis.

From the immediately practical point of view, it is impossible to doubt that a postponement of the age of attack is what public health action should seek to secure, combined with amelioration of those particular conditions of over-

crowding which are especially helpful to the efficiency of droplet infection.

#### RECOMMENDATIONS FOR FURTHER STUDY

As usual, Creighton and Hirsch must head the list. Dr. J. L. Halliday's investigation of the relationship between housing conditions and the fatality of measles (Medical Research Council's Special Report Series, No. 120), the late H. E. Soper's mathematical paper (*Journal of the Royal Statistical Society*, Vol. XCII, 1929, pp. 34-61), and my not *very* but perhaps a *little* mathematical study of infectiousness (*Journal of Hygiene*, 1931, Vol. XXI, p. 336) might be read. The paper of Dr. Stocks and Miss Karn *must* be read (*Annals of Eugenics*, Vol. III, 1928, p. 361).

## DIPHTHERIA

THE history of scarlet fever is confused, intrinsically confused, with that of diphtheria, although there is no doubt that at least as early as the seventeenth century, and considerable probability that in the days of the Roman Empire, epidemics of sickness occurred which, had *we* observed them, we should certainly have described as diphtheria.

A special confusion was introduced in the middle of the eighteenth century by a Scottish physician, Francis Home, who satisfied himself and his British contemporaries that a particular syndrome, the hoarse crowing sound on inspiration, which he called *croup* (the word is derived from a root found in all Teutonic languages and is onomatopaeic), was the essential differentia of a "new" disease. This error was not rectified for more than sixty years, and, indeed, produced medical statistical confusion for much longer.

The—as we now believe—correct doctrine of the essential nature of diphtheria is due to Bretonneau of Tours, *clarum et venerabile nomen*. Bretonneau had special opportunities for observation; it seems clear that almost down to the middle of the nineteenth century, diphtheria—to give it the name first introduced into English statistical nomenclature by Farr in 1858—was not a serious cause of illness in any west European country but France. From the middle of the nineteenth century, diphtheria increased in importance in Great Britain. At first it was somewhat overshadowed as a cause of illness and death by scarlet fever. Both had maxima in the quinquennium 1861–5, but scarlet fever killed almost twice as many as diphtheria. Since then, although both illnesses have become less deadly, scarlet fever has decreased in importance so much faster than diphtheria that by 1927 the rate of mortality due to the latter was almost fivefold the rate due to the former. In nearly all other European countries diphtheria now kills many more children than scarlet fever; thus in Germany in 1926 only 964 deaths were assigned to scarlet fever but 2,189 to diphtheria. In that year Italy alone of the greater

Powers had practically equal numbers of deaths assigned to the two illnesses.

Diphtheria in England has followed a rule which might almost pass for a law of epidemiology, viz. that when first prominent—whether really for the first time or for the first time after a long interval of torpor—the incidence is as great in the country districts as in towns or actually greater in the villages than the towns, and then as time passes the sickness tends to leave the country and linger in the towns. That sequence has been noted in the history of plague and smallpox; it is obvious in that of diphtheria. Eighty years ago diphtheria took a much heavier toll of the sparsely populated districts than of the towns. Now the rate of mortality in county boroughs is twice that upon rural districts.

A clear account of the epidemiological position of the generation before ours, the generation which was growing old when bacteriology was a child, is contained in the Milroy Lectures of 1891 delivered by Richard Thorne-Thorne (later Medical Officer to the Local Government Board, the successor of Sir George Buchanan the elder and the predecessor of Sir William Power). Although it was still not possible to dismiss peremptorily the doctrine of, if not spontaneous generation, at least transformation of some morbid substance present in the soil or in the air of sewers, it was quite fully realized that case-to-case infection and mediate infection by way of contaminated milk were far the most important mechanisms. Thorne-Thorne himself in a study of an epidemic at Great Coggeshall (a small Essex town) in 1875-6 and Power in reports on epidemics at Radwinter in Essex in 1876 and at Pirbright in Surrey in 1883 drew pictures of what may be called the normal epidemiology of diphtheria which have not been improved upon by later artists. The normal course of events is that one has a history of disseminated illness—"bad throats," feverish attacks, with perhaps a few deaths; this phase is likely to be interrupted by exacerbations, a heaping up of cases or a tendency for the clinical type to become more severe. There is seldom anything dramatic about the business, no great turns of fortune as in, for instance, a water-borne typhoid outbreak. That one is really dealing with case-to-case spread may indeed be surmised, but to bring adequate epidemiological proof is not always easy. Power's handling of the data in the Pirbright pre-

valence is, I think, worth close study. He had formed the general impression that the illness was spread by school contact and this is the way in which he tested the hypothesis. He compared the attack-rate in age groups upon members of households which had had at least two cases (*excluding the first cases*) with the age distribution of first attacks and obtained the following statistics :

TABLE 24

Age Periods	In Families already Invaded			First Attacks in Families		
	Persons Living at Age Periods	Numbers Attacked	Attacks Per Cent	Persons Living at Age Periods	Numbers Attacked	Attacks Per Cent
0-3 years ..	22	2	9.0	52	1	1.8
3-12 years ..	59	23	38.0	148	37	25.0
12-15 years ..	22	7	31.8	57	5	10.8
Over 15 years ..	148	20	13.5	444	9	2.0

(Taken from *Diphtheria, its Natural History and Prevention*, R. Thorne-Thorne, Milroy Lectures, 1891, p. 118.)

From this Table it is seen that, relatively to other age groups, that of school age is much more likely to be first attacked when there is no domestic source of infection. Under those conditions children of three to twelve are attacked at more than twice the rate of older children (beyond school age), while, when cases have already occurred in the family, the attack-rate upon older exposed children is not much less than upon those of school age. Since even with a domestic focus of infection the putative school influences would tell against the children of appropriate age, the comparison would be perhaps more striking still could the data be further subdivided. Power then showed that if the attack-rates upon children aged three to twelve years who were or who were not attending school and had not already been attacked were compared, the school-attending children suffered a far heavier incidence. He noted that the data were few, but urged that "the indication which they furnish is too uniform to be mistaken."

The detailed mechanism of such school infections has been worked out since Power's time, with especial clearness by Dudley; what in 1883 was only inferential is now matter of description.

In such ways the personal factors of spreading were brought to light—I have cited only familiar English work of the last generation, but might have taken Bretonneau's studies of sixty years before so far as the elucidation of principles is concerned. Just as the enjoyment of detective fiction (of which I am a pas-

TABLE 25

Week Ending	Inner Circle			Outer Ring		
	Households Newly Invaded	Persons Newly Attacked	Deaths	Households Newly Invaded	Persons Newly Attacked	Deaths
March 9th ..	1	1	—	1	1	—
March 16th ..	4	6	—	1	6	—
March 23rd ..	2	4	1	—	—	—
March 30th ..	4	4	3	1	2	—
April 6th ..	—	1	1	2	2	1
April 13th ..	—	1	—	2	3	—
April 20th ..	2	6	—	—	1	—
April 27th ..	5	8	—	1	2	—
May 4th ..	8	16	1	2	2	—
May 11th ..	7	20	1	—	—	—
May 18th ..	41	104	1	5	7	—
May 25th ..	14	35	13	1	2	1
June 1st ..	5	12	4	3	3	2
June 8th ..	3	7	3	—	2	4
June 15th ..	2	5	2	1	1	—
Totals in 15 weeks	98	230	30	20	34	8

(Taken from W. H. Power's report to the Local Government Board on Epidemic Prevalence of Diphtheria in North London,\* Table II, 1878.)

sionate admirer) is marred by a foreign and unfamiliar atmosphere—one pines for the fictitious Scotland Yard when one is conducted through the fictitious Sûreté—it is (to me) easier to follow epidemiological plays when the characters move on a familiar English stage. On that account I shall again bring forward the work of Power in tracing communal factors of spreading, other than that of schools.

\* *Parliamentary Report on Medical Subjects*, 1878.

Power's report on an outbreak of throat illness in Kilburn and St. John's Wood in 1878 is an elegant piece of epidemiological detection.

The outbreak was a long-drawn-out affair covering more than fifteen weeks, but had this of the dramatic, that of 118 invaded households 78 were attacked within a particular period of four weeks (Table 25).

Power noticed that if two circles were struck around a particular point, the former with a radius of  $\frac{1}{2}$  mile, the latter with a radius of 1 mile, the inner circle contained 98 newly invaded households (period of observation from March 9 to June 15, 1878) with 230 attacked persons and 30 deaths. The ring left when the area of the inner circle was subtracted from that of the other circle contained 20 newly invaded households, 34 newly attacked persons, 8 deaths. It will be seen that there is a very special incidence in May. It equally appears that some sharply circumscribed factor affecting the inner circle must have been important.

The investigator notes that "all that previous research has justified us in affirming is that the disease has a power of spread from person to person, and has also a faculty of development out of an antecedent prevalence of throat illness, the diphtheretic character of which may not, until a certain stage of prevalence has been reached, be affirmed." The investigator notes that a study of 111 infected households elicited the result that in 77 the first sufferers had neither had communication with any case of antecedent throat illness nor attended school within one week before date of attack.

The water supply of the infected houses was good and shared by London districts not affected.

The sewerage of part of the area was open to serious criticism. Owing to the coalescence of two main sewers to form a single circular sewer of less cross-section there was possibility of back-pressure, and the investigator found proof of such backflow when after heavy rainfall on April 10th and 11th back-current was actually observed by the Hampstead surveyor and there was serious flooding of basements in the district. Since the house drains were most imperfectly ventilated and trapped there was ample opportunity for sewer gas to enter the houses.

TABLE 26

Week Ending	Special Sewage Area. Houses, 2,000	Adjoining Districts	
		Inner Circle. Houses, 700	Outer Ring. Houses, 2,700
March 9th .. .. .	1	—	1
March 16th .. .. .	4	—	1
March 23rd .. .. .	2	—	—
March 30th .. .. .	4	—	1
April 6th .. .. .	—	—	2
April 13th .. .. .	—	—	2
April 20th .. .. .	1	1	—
April 27th .. .. .	4	1	1
May 4th .. .. .	6	2	2
May 11th .. .. .	7	—	—
May 18th .. .. .	38	3	5
May 25th .. .. .	13	—	2
June 1st .. .. .	3	3	2
June 8th .. .. .	2	1	—
June 15th .. .. .	1	1	1
Total, 15 weeks ..	86	12	20

(W. H. Power, op. cit.)

TABLE 27

Periods	Households per 1,000 Attacked by Throat Illness	
	Special Sewage Area. Houses, 2,000	Other Parts of Infected District. Houses, 3,400
Whole outbreak .. .. .	43·0	9·2
Six weeks to date of sewer obstruction ..	5·5	2·0
Four weeks succeeding date of sewer obstruction .. .. .	9·0	2·0
Fifth week from date of sewer obstruction ..	19·0	2·3
Rest of the outbreak .. .. .	9·5	2·9

(W. H. Power, op. cit.)

Tables 26 and 27 set out the comparison of the area to which this criticism applies with the rest of the implicated area and contrasts the temporal incidence after the period of sewer obstruction in April referred to. The investigator notes that there is a much heavier incidence upon the area of defective sewerage, although the interval between the obstruction and the increased incidence is longer than clinical experience would suggest to be the incubation period of diphtheria, still, *prima facie* a case is made.

One now comes to milk distribution.

TABLE 28

## SCHEME OF MR. X'S MILK DISTRIBUTION

Milk supply derived from—			
Dairy X <sup>1</sup>		Dairy X <sup>2</sup>	
(yield about 80 gallons)		(yield about 54 gallons)	
by Mr. A	.. .. 47	by Mr. M	9
by Mr. B	.. .. 24	by Mr. N	19
by Messrs. c	.. ..	by Mr. O	10
by Messrs. d	.. ..	by Mr. P	2½
by Messrs. e	.. ..	by Mr. Q	13
etc.			

(W. H. Power, op. cit.)

The milk supply of the inner circle was as follows: 236 households by A, 237 by B, 2,227 by other retailers. Of the first group 37 or 156 per 1,000, of the second 31 or 130 per 1,000, of the third 30 or 13 per 1,000 had cases of throat illness. A similar contrast existed in the outer zone. Within the zone of special sewerage, 148 per 1,000 of households supplied by A or B had cases, the customers of other milkmen 11 per 1,000.

Table 29 (p. 204) shows the explosive outburst on the A and B customers, also that prior to this outburst there was no special incidence at all on A and B clients. It also appeared that other throat illness had a peculiar distribution tending, before the special outburst, to affect a retailer who was supplied from one of the two X farms.

Table 30 (p. 204) shows a similar differential incidence upon the customers of another retailer of A milk made out in other London districts.

The train of circumstantial evidence connecting the milk supply

TABLE 29  
SHOWING THE NUMBER OF HOUSEHOLDS INVADDED WEEK BY WEEK IN EACH GROUP REFERRED TO

	March				April				May				June	
	9	16	23	30	6	13	20	27	4	11	18	25	1	8
Households supplied by retailers other than Mr. A or Mr. B ..														
Households supplied by Mr. A or Mr. B only ..	1	5	2	5	2	2	1	2	4	1	6	4	5	2
	1	-	-	-	-	-	1	4	6	6	40	11	3	1

(W. H. Power, op. cit.)

TABLE 30

Households Obtaining Milk from	Period Antecedent to Main Outburst								Period Corresponding to Main Outburst							
	March				April				Households Invaded in Period				May			
	9	16	23	30	6	13	20	27	4	11	18	25	1	8	15	Households Invaded in Period
X sources :																
Messrs. C, d, e, etc. (X <sup>1</sup> business) ..	-	-	-	-	-	-	-	1	-	-	1	1	1	-	-	3
Mr. M (X <sup>1</sup> business) ..	1	2	1	4	2	1	1	12	1	-	-	-	-	-	-	1
Sources other than X ..	-	3	1	1	-	1	1	7	3	1	5	3	4	2	2	20
Total ..	1	5	2	5	2	2	1	20	4	1	6	4	5	2	2	24

(W. H. Power, op. cit.)

with the outbreak of throat illness is as complete as we are ever likely to find in evidence of this class. Since Power's day, bacteriological verification has been obtained in similar cases.

In these ways were laid the foundations of our present beliefs, and if we had not learned much more of the intimate biology of diphtheria than of scarlet fever there would be little more to add. From the epidemiological point of view we should class the two illnesses together, in respect of their methods of spread and the available means of prophylaxis, and should merely regret that the methods had been associated with less practical success in diphtheria than in scarlet fever. We should note that, like scarlet fever, diphtheria has a seasonal trend. Normally the increase begins in England a little earlier in the year—say in the thirty-fifth rather than the thirty-seventh week—while the maximum (usually between the fortieth and forty-fifth week of the year), like that of scarlet fever, is about double the minimum incidence. We should also note that larger prevalences, epidemics, occur at intervals of several years, that increase of scarlet fever is usually associated with increase of diphtheria, but that the secular variation of diphtheria is on the whole greater than that of scarlet fever. Epidemics of diphtheria are more frequent than epidemics of scarlet fever, but numerically less imposing.

That would be almost all worth while saying in such an account as this if we knew no more of the biology of diphtheria than of scarlet fever. But we do know a great deal more. Not only can we ascertain whether a once infected person continues to harbour the bacillus determining the individual pathogenic process and so gain knowledge of the potential sources of case-to-case infection in a community; we can also, by means of a test first introduced by Schick, make a rough evaluation of the measure of resistance of individual members of a group and can take steps to increase that resistance. A large literature of these subjects has grown up which is adequately summarized in a recent publication of the Medical Research Council. I have no intention of going over again badly what has been already done well, and shall only refer to a few practically important points.

In 1919, Hartley and Martin\* published a study of the rate of decrease among bacillus carriers of particular interest. Their

\* *Proc. Roy. Soc. Med.*, 1919-20, Vol. XIII (Sect. of Epidem.), p. 277.

subjects were young soldiers convalescent from diphtheria and under observation in a hospital for infectious diseases. The throats were examined, and only if three examinations at intervals of twenty-four hours failed to reveal *C. diphtheriae* was an individual transferred from the carrying to the non-carrying group. The second column of Table 31 records the numbers still carrying at intervals of five days from admission, the third column the numbers which would have been found had carriers ceased to carry in geometrical progression, the rate of decrement being approximately 5 per cent per diem.

TABLE 31  
CONVALESCENT SOLDIERS IN FRANCE

Days after Admission	Observed Carriers	Calculated Number of Carriers
5	392	398
10	302	310
15	232	242
20	194	189
25	156	147
30	118	117
35	92	89
40	70	70
45	52	54
50	41	42

The agreement is excellent. These young men obeyed the compound interest law, or, as Dr. Brownlee would have said, the law of the monomolecular reaction, with respect to their discharges from the ranks of carriers.

If this were the "real" law of the phenomenon, it would follow not only that the probability that a person who is carrier at the end of  $n$  days will cease to be a carrier after  $n + 1$  days is exactly the same as the probability that he who has carried  $n + m$  days will cease to carry one day later, but that, provided the exposed to risk are sufficiently numerous, some will carry to the end of their days.

A thorough study of the time-relations of carrying in patients treated in the hospitals of the Metropolitan Asylums Board was

published by Thomson, Mann, and Marriner in the Board's Annual Report for 1928-9.\* The plan followed was this. When a patient was admitted to hospital, cultures were made and a case only reckoned negative if three successive cultures at daily intervals were all negative. A culture was taken in the second and another in the third week of residence. Thereafter cultures were taken twice weekly, and a patient was only transferred to the non-carrier class if the cultures had been negative over three weeks. Of 1,726 patients with positive throat cultures, only 865 still gave positive results in the second week, viz. 50.1 per cent. Of these 610 still carried in the third week 70.5 per cent. The numbers remaining in each successive week were 356, 218, 132, 86, 45, 27, 12, and 7. If we take the ratio of each number to its predecessor, viz.  $356 : 610$ ,  $218 : 356$ , etc., we reach the series 0.58, 0.61, 0.61, 0.65, 0.52, 0.60, 0.44, 0.58.

These ratios are not constant, but, so long as the numbers are large, do not vary widely. In fact if we use 0.6 as a common multiplier, i.e. multiply 610 by 0.6, the product by 0.6, and so on, we shall have the following series (the number in brackets after each figure is the true value): 366 (356), 220 (218), 132 (132), 79 (86), 47 (45), 28 (27), 17 (12), 10 (7); which is not a bad result and would correspond to a daily decrement of about 8 per cent. In hospitalized children, then, *after the first three weeks of observation* it seems that a geometrical law of decrement holds. When the nose either alone or as well as the throat is infected, the rate of transfer from the infected to the uninfected class is slower. Thus in Thomson, Mann, and Marriner's series of 1,240 nose or nose and throat carriers, 942 were still infected in the second week, and of these 783 were still carrying in the third week. The decrement in later weeks is at the rate of about 5.5 per cent per diem. In younger children the rate of decrement is slower than in older children or adults. Thus, of children under 7 who were nose or nose and throat carriers, 85.4 per cent had ceased to be carriers in eight weeks, of children aged 7-13, 88.4 per cent, and of persons over 13, 94 per cent.

It follows that in a very large population a few carriers may be expected to hold out a very long time, theoretically for ever. If carriers are, indeed, the means of carrying on the sacred fire,

\* P. 304 et seq.

that fire is never likely to burn itself out in a population of millions. With respect to the distribution of immunity in a group, Dudley's observations in the Royal Naval School at Greenwich are of special interest. He showed that the proportion of boys who were Schick-positive decreased with length of residence. At entrance less than 60 per cent were immune (as decided by the test); after six months to two years the percentage had risen to 85 per cent; while those who had been in the school from two and a half years to four and a half years—the oldest inhabitants—consisted of 95 per cent immunes. Dudley noted that when the percentage of non-reactors (i.e. immunes) was plotted against time the increments seemed not to be continuous but only to occur after outbursts of clinical diphtheria in the school. He inferred that the level of immunity does not rise without the presence in the group of active disease. I do not think his data, valuable as these were, suffice to make that inference quite safe. Indeed, the change in the proportion of immunes with increasing length of residence does not differ very much (except as requiring a too large proportion of immunes amongst new-comers) from what we should expect if it changed logarithmically, just as if the proportional law of change were the same as that observed in the lapsing from the carrier state. The point, however, is too subtle to be worth discussion here. What is clear is that the average immunity level, within a community such as this, changes in time, the change being a function of the previous history of entrants to the community and of the conditions prevailing therein. The effects of introducing massive infection will depend upon the particular level of immunity reached. It has been found that children of the hand-working classes contain, age for age, a higher proportion of immunes than those of more prosperous parents. Such a fact helps to account for differences in the evolution of epidemics in schools of different social classes.

In addition to variation in degree of exposure to infection it is probable, although the evidence is not free from ambiguity, that differences of natural and heritable resistance are of importance. This is suggested by an apparent correlation of the Schick reaction with the character of the reactor's blood-grouping. It seems to be established that the character of the blood with respect to so-called iso-agglutination is heritable, and, should it be confirmed that it is this which is the link of association when

members of the same family are all positive, or all negative, Schick reactors, the obvious explanation of the facts on the basis of common environment fails.

We must now realize that the course of events within a community is a function of *at least* three variables: previous exposure to infection, physiological constitution, conditions of life. Since by inoculating an appropriate mixture of toxin and anti-toxin it is certain that individual resistance can be raised, an obvious suggestion is that outbreaks of diphtheria might be prevented by raising the resistance of *all* susceptibles exposed to risk. Such a measure has been tried with success in several small, closed or semi-closed communities and is now of practical administrative importance. Encouraged by such results, immunizing upon the grand scale has been adopted in some cities, notably New York.

Very recently Dudley has suggested that the active immunization of part of a group is not so wholly beneficial an action from the group point of view as had at first been thought. It seems to have been made probable that the percentage of actively immunized persons who carry virulent organisms in their throats is much above the normal average. Hence, if a population is only partly immunized—if, for example, children of school age are immunized, but not their brothers and sisters below school age—then, under normal family conditions, it may happen that the total risk to the group is greater than if one had not played the part of (partial) providence. Suppose one had a group of one hundred individuals and that normally five would be infected with some disease, our rate of loss over the group is 5 per cent. Suppose now we render fifty completely immune from the disease, but through their agency increase the risk of the remaining fifty from one in twenty to one in ten; then the group will sustain, as before, an overall percentage of loss of five. From the crowd point of view the immunization is a pure waste of effort. That is a crude exaggeration of Dudley's argument, but it is an argument, based upon definite experimental evidence.

#### RECOMMENDATIONS FOR FURTHER STUDY

Of the older books, E. H. Greenhow's *On Diphtheria* (1860) and R. Thorne-Thorne's *Diphtheria* (1891) are of special value; both give ample

references to the earlier literature. The recent literature is, of course, enormous. S. F. Dudley's report (Medical Research Council's Special Report Series, No. 111) should be read and Chapter LIX of Topley and Wilson's *The Principles of Bacteriology and Immunity* (1929); the latter supplies other useful references. Dr. J. Graham Forbes' report (Medical Research Council, Special Report Series, No. 115) is another useful and instructive monograph.

## VI

### SCARLET FEVER

THE epidemiological history of scarlet fever is interesting from several points of view, most perhaps as affording us the best instance in epidemiology of change of type. The early history of prevalences is as obscure as anything in our subject; it is possible that outbreaks were seen by the Near Eastern practitioners of the Arabian school, and certain that clinically the *morbilli* of the Arabists and mediaeval physicians had a wider diagnostic connotation than our measles, but no clear account of any *prevalence* wherein a fiery rash was a characteristic physical sign (*totem corpus ignitum appareat*) has reached us earlier than that of Ingrassia of Palermo written in the middle of the sixteenth century. Ballonius was probably familiar with an epidemiological distinction between measles and scarlet fever, and Döring of Breslau wrote a quite satisfactory clinical account of *cases* of scarlet fever when Sydenham was a small child. Döring (or perhaps his father-in-law Sennart, who published his notes) did not separate scarlet fever from measles as a "different disease," a step taken by Sydenham in his over-praised note on *Febris Scarlatina* first published in 1676.

By the end of the seventeenth century the clinical, and, to some extent, epidemiological concept of scarlet fever was common medical property, but there was by no means an end of epidemiological confusion. Clinicians of the eighteenth century were clear about *Scarlatina simplex*, or what we should now call mild scarlet fever without complications, but to distinguish the prevalences of scarlatinal and malignant *anginas* reported upon by them and to classify these to scarlet fever or diphtheria is a task which has baffled the most learned medical historians; indeed, one of the most philosophical of them, Charles Creighton, doubted whether any such distinction were scientific at all—he leaned to the view that scarlet fever and diphtheria developed from a common ancestor. There is more than a touch of arbitrariness in any identifications even from so recent a period as the middle of the eighteenth century, but the general evidence

is strong enough to warrant Hirsch's remark that, in comparison with measles, scarlet fever has appeared much more rarely in great waves of prevalences, or at quasi-regular intervals. It is also strong enough to warrant the remark that *as a cause of mortality* scarlet fever has varied greatly. Such variations occurred long before our time.

There is little doubt that in England in the last years of the eighteenth century, scarlet fever was much more *deadly* than it had been a quarter of a century before or was again a quarter of a century later, but no reason to suppose that its prevalence was especially great. A comparison between the end of the eighteenth century and twenty years later can be adequately sustained because for the years 1796-1800 we have the very competent observations of Willan, while from 1804-16 Bateman, another good observer, kept records of the prevalent diseases in London. The difference of tone of the observers is conspicuous. In November 1798 we find Willan writing: "The fatal cases of scarlatina were in the month of November, when the disease was more extended, and more virulent than any period within my recollection since the years 1786, 1787." Contrast Bateman writing in the autumn of 1814: "The measles and scarlet fever have been very prevalent; and the former, in a few cases, were attended with considerable affections of the chest. The scarlatina has been, in all the cases, accompanied by sore throat; in the adults, indeed, in two or three families, the throat, as is usual, was the only seat of the disease, as the rash did not appear on the skin. Under cool treatment, which, however, is often very imperfectly accomplished in the close and crowded apartments of the poor, these cases have uniformly done well."

A *prevalent* disease in both epochs; but in the former malignant, in the latter trivial. From shortly after the turn of the century for nearly twenty-five years, English practitioners saw plenty of mild scarlet fever; their patients did well and the doctors congratulated themselves upon the superiority of their methods to those of their fathers. But in the thirties of the century—when many other epidemiological portents, cholera, influenza, even smallpox, blazed—there was a change for the worse, and for more than a generation, indeed down to 1875, scarlet fever ranked without dispute as "the leading cause of death among the infec-

T.  
SCARLET FEVER

Years	Standardized Death- rate per 1,000,000	0-5	5-10	10-15	15-20	20-25
<i>Males</i>						
1861-70	(867)	550 ± 3.3	257 ± 2.9	54 ± 1.5	17 ± 0.9	9 ± 0.7
1871-80	(638)	565 ± 3.6	245 ± 3.1	50 ± 1.6	17 ± 1.0	9 ± 0.8
1881-90	(303)	564 ± 4.9	205 ± 4.2	40 ± 2.2	14 ± 1.2	8 ± 1.0
1891-1900	(152)	562 ± 6.6	229 ± 5.6	51 ± 3.0	25 ± 2.2	14 ± 1.8
1901-10	(110)	533 ± 7.3	250 ± 6.5	55 ± 3.6	31 ± 2.8	15 ± 2.0
1921-4	(35)	459 ± 12.5	256 ± 11.8	73 ± 6.9	44 ± 5.5	27 ± 4.7
<i>Differences</i>						
1861-70, 1901-10	—	— 17 ± 8.0	— 7 ± 7.1	+ 1 ± 3.9	+ 14 ± 2.9	+ 6 ± 2.1
1861-70, 1921-4	—	— 91 ± 12.9	— 1 ± 12.1	+ 19 ± 7.1	+ 27 ± 5.6	+ 18 ± 4.8
1871-80, 1901-10	—	— 32 ± 8.1	+ 5 ± 7.2	+ 5 ± 3.9	+ 14 ± 3.0	+ 6 ± 2.2
1871-80, 1921-4	—	— 106 ± 13.0	+ 11 ± 12.2	+ 28 ± 7.1	+ 27 ± 5.6	+ 18 ± 4.8
<i>Females</i>						
1861-70	(847)	534 ± 3.4	255 ± 2.9	63 ± 1.7	19 ± 1.0	13 ± 0.8
1871-80	(612)	556 ± 3.8	242 ± 3.1	54 ± 1.7	17 ± 1.0	11 ± 0.8
1881-90	(298)	545 ± 5.1	257 ± 4.3	53 ± 2.3	13 ± 1.2	9 ± 1.0
1891-1900	(152)	548 ± 6.7	235 ± 5.6	56 ± 3.1	18 ± 1.8	15 ± 1.7
1901-10	(107)	517 ± 7.6	255 ± 6.7	64 ± 3.9	23 ± 2.4	17 ± 2.0
1921-4	(37)	406 ± 12.3	273 ± 11.9	97 ± 7.7	44 ± 5.4	34 ± 4.9
<i>Differences</i>						
1861-70, 1901-10	—	— 17 ± 8.3	— 0	+ 1 ± 4.3	+ 4 ± 2.6	+ 4 ± 2.2
1861-70, 1921-4	—	— 128 ± 12.8	+ 18 ± 12.2	+ 34 ± 7.9	+ 26 ± 5.5	+ 21 ± 5.0
1871-80, 1901-10	—	— 39 ± 8.5	+ 13 ± 7.4	+ 10 ± 4.3	+ 6 ± 2.6	+ 6 ± 2.2
1871-80, 1921-4	—	— 150 ± 12.9	+ 31 ± 12.3	+ 43 ± 7.9	+ 27 ± 5.5	+ 23 ± 5.0

(Taken from "Statistical Study of Scarlet Fever and Diphtheria," H. M. Woods, *Journal of Hygiene*, Vol. XXVIII, No. 2, 1908 p. 120.)

is strong enough to warrant Hirsch's remark that, in comparison with measles, scarlet fever has appeared much more rarely in great waves of prevalences, or at quasi-regular intervals. It is also strong enough to warrant the remark that *as a cause of mortality* scarlet fever has varied greatly. Such variations occurred long before our time.

There is little doubt that in England in the last years of the eighteenth century, scarlet fever was much more *deadly* than it had been a quarter of a century before or was again a quarter of a century later, but no reason to suppose that its prevalence was especially great. A comparison between the end of the eighteenth century and twenty years later can be adequately sustained because for the years 1796-1800 we have the very competent observations of Willan, while from 1804-16 Bateman, another good observer, kept records of the prevalent diseases in London. The difference of tone of the observers is conspicuous. In November 1798 we find Willan writing: "The fatal cases of scarlatina were in the month of November, when the disease was more extended, and more virulent than any period within my recollection since the years 1786, 1787." Contrast Bateman writing in the autumn of 1814: "The measles and scarlet fever have been very prevalent; and the former, in a few cases, were attended with considerable affections of the chest. The scarlatina has been, in all the cases, accompanied by sore throat; in the adults, indeed, in two or three families, the throat, as is usual, was the only seat of the disease, as the rash did not appear on the skin. Under cool treatment, which, however, is often very imperfectly accomplished in the close and crowded apartments of the poor, these cases have uniformly done well."

A *prevalent* disease in both epochs; but in the former malignant, in the latter trivial. From shortly after the turn of the century for nearly twenty-five years, English practitioners saw plenty of mild scarlet fever; their patients did well and the doctors congratulated themselves upon the superiority of their methods to those of their fathers. But in the thirties of the century—when many other epidemiological portents, cholera, influenza, even smallpox, blazed—there was a change for the worse, and for more than a generation, indeed down to 1875, scarlet fever ranked without dispute as "the leading cause of death among the infec-

TABLE 32

## SCARLET FEVER

Years	Standardized Death-rate per 1,000,000	0-5	5-10	10-15	15-20	20-25
<i>Males</i>						
1861-70	(867)	550 ± 3.3	257 ± 2.9	54 ± 1.5	17 ± 0.9	9 ± 0.7
1871-80	(638)	565 ± 3.6	245 ± 3.1	50 ± 1.6	17 ± 1.0	9 ± 0.8
1881-90	(303)	564 ± 4.9	205 ± 4.2	40 ± 2.2	14 ± 1.2	8 ± 1.0
1891-1900	(152)	562 ± 6.6	229 ± 5.6	51 ± 3.0	25 ± 2.2	14 ± 1.8
1901-10	(110)	533 ± 7.3	250 ± 6.5	55 ± 3.6	31 ± 2.8	15 ± 2.0
1921-4	(35)	459 ± 12.5	256 ± 11.8	73 ± 6.9	44 ± 5.5	27 ± 4.7
<i>Differences</i>						
1861-70, 1901-10	—	— 17 ± 8.0	— 7 ± 7.1	+ 1 ± 3.9	+ 14 ± 2.9	+ 6 ± 2.1
1861-70, 1921-4	—	— 91 ± 12.9	— 1 ± 12.1	+ 19 ± 7.1	+ 27 ± 5.6	+ 18 ± 4.8
1871-80, 1901-10	—	— 32 ± 8.1	+ 5 ± 7.2	+ 5 ± 3.9	+ 14 ± 3.0	+ 6 ± 2.2
1871-80, 1921-4	—	— 106 ± 13.0	+ 11 ± 12.2	+ 28 ± 7.1	+ 27 ± 5.6	+ 18 ± 4.8
<i>Females</i>						
1861-70	(847)	534 ± 3.4	255 ± 2.9	63 ± 1.7	19 ± 1.0	13 ± 0.8
1871-80	(612)	556 ± 3.8	242 ± 3.1	54 ± 1.7	17 ± 1.0	11 ± 0.8
1881-90	(298)	545 ± 5.1	257 ± 4.3	53 ± 2.3	13 ± 1.2	9 ± 1.0
1891-1900	(152)	548 ± 6.7	235 ± 5.6	56 ± 3.1	18 ± 1.8	15 ± 1.7
1901-10	(107)	517 ± 7.6	255 ± 6.7	64 ± 3.9	23 ± 2.4	17 ± 2.0
1921-4	(37)	406 ± 12.3	273 ± 11.9	97 ± 7.7	44 ± 5.4	34 ± 4.9
<i>Differences</i>						
1861-70, 1901-10	—	— 17 ± 8.3	— 0	+ 1 ± 4.3	+ 4 ± 2.6	+ 4 ± 2.2
1861-70, 1921-4	—	— 128 ± 12.8	+ 18 ± 12.2	+ 34 ± 7.9	+ 25 ± 5.5	+ 21 ± 5.0
1871-80, 1901-10	—	— 39 ± 8.5	+ 13 ± 7.4	+ 10 ± 4.3	+ 6 ± 2.6	+ 6 ± 2.2
1871-80, 1921-4	—	— 150 ± 12.9	+ 31 ± 12.3	+ 43 ± 7.9	+ 27 ± 5.5	+ 23 ± 5.0

(Taken from "Statistical Study of Scarlet Fever and Diphtheria," H. M. Woods, *Journal of Hygiene*, Vol. XXVIII, No. 2, 1928, p. 150.)

tious maladies of childhood." The high-water mark was reached in the year 1863 when the rate of mortality was 1,478 per 1,000,000 living at all ages, and 3,966 upon those living at ages under fifteen. The scale of the mortality is illustrated by Farr's statistics. According to him, in the most unhealthy district of England, the registration district of Liverpool, of every 1,000,000 children born, 26,818 died of scarlet fever before attaining the age of five years. In England as a whole the proportion was 17,959. In the *healthy districts*, that is districts selected on account of their low general death-rate, 11,373 died of scarlet fever before the age of five out of every 1,000,000 born, while the quota of whooping-cough was 9,650, of measles 5,257, and of diphtheria 4,184. These figures are sufficiently impressive, but a study of memoirs and diaries of the time will bring the facts more vividly before one. The famous Dr. Tait, for instance—who was afterwards Archbishop of Canterbury—lost five of his six children within a month. Mr. Maclagan—afterwards Archbishop of York—lost his wife of scarlet fever, and the great teacher of medicine, Sir Thomas Watson, wrote of scarlet fever that "sometimes the disorder defies all treatment and the deadliest forms of plague are not more fatal."

Some fifty years ago, scarlet fever entered upon another phase of its secular history; it continued to be prevalent enough, but its killing and maiming powers began to decline, and have continued to decline, so that at present its effect upon the death-rate is small.

In declining, the improvement has not been uniform, but greater in childhood than in later life.

Table 32 which expresses the rate of mortality in any age group as a percentage of the standardized rate of mortality of the decennium brings this out. Thus in 1861-70 the rate of mortality amongst males aged 0-5 was five and a half times the all-ages rate, high as that was. In 1921-4 it was only four and a half times the very much reduced all-ages rate. At ages 10-15, for instance, the rate was a little more than half the all-ages rate in 1861-70, almost three-quarters of it in 1921-4. This has not happened in diphtheria (Table 33); there the tendency has been for a *relative* concentration of mortality in childhood, although not in the earliest but in the second quinquennium of life.

The decline of scarlet fever as a killing disease has been imme-

TABLE 33  
DIPHTHERIA

Years	Standardized Death- rate per 1,000,000	0-5	5-10	10-15	15-20	20-25
<i>Males</i>						
861-70	(155)	490 ± 7.6	219 ± 6.4	69 ± 4.1	37 ± 3.2	23 ± 2.7
871-80	(102)	465 ± 8.7	252 ± 7.7	71 ± 4.8	27 ± 3.1	20 ± 3.0
881-90	(140)	491 ± 7.1	266 ± 6.3	60 ± 3.5	25 ± 2.4	14 ± 2.0
891-1900	(248)	560 ± 6.0	248 ± 4.7	45 ± 2.5	15 ± 1.8	8 ± 1.3
901-10	(178)	540 ± 5.7	277 ± 5.3	49 ± 2.6	11 ± 1.3	6 ± 1.0
921-4	(109)	480 ± 7.1	312 ± 7.1	79 ± 4.1	16 ± 2.0	4 ± 1.0
<i>Differences</i>						
861-70, 1901-10	—	+ 50 ± 9.5	+ 58 ± 8.3	- 20 ± 4.9	- 26 ± 3.5	- 17 ± 2.9
861-70, 1921-4	—	- 10 ± 10.4	+ 93 ± 9.6	+ 10 ± 5.8	- 27 ± 3.8	- 19 ± 2.9
871-80, 1901-10	—	+ 75 ± 10.4	+ 25 ± 9.3	- 22 ± 5.5	- 16 ± 3.4	- 14 ± 3.2
871-80, 1921-4	—	+ 15 ± 11.2	+ 60 ± 10.5	+ 8 ± 6.3	- 17 ± 3.3	- 16 ± 3.2
<i>Females</i>						
861-70	(176)	444 ± 7.2	256 ± 6.4	94 ± 4.4	35 ± 2.9	23 ± 2.4
871-80	(114)	417 ± 8.2	287 ± 7.7	92 ± 5.1	33 ± 3.3	19 ± 2.5
881-90	(156)	444 ± 6.7	304 ± 6.3	74 ± 3.7	24 ± 2.3	13 ± 1.7
891-1900	(260)	514 ± 5.1	286 ± 4.6	53 ± 2.3	14 ± 1.2	8 ± 1.0
901-10	(189)	498 ± 5.7	319 ± 5.4	50 ± 2.6	11 ± 1.3	5 ± 1.0
921-4	(115)	431 ± 7.0	362 ± 7.2	81 ± 4.0	16 ± 1.9	8 ± 1.4
<i>Differences</i>						
861-70, 1901-10	—	+ 54 ± 9.2	+ 63 ± 8.4	- 44 ± 5.1	- 24 ± 3.2	- 18 ± 2.5
861-70, 1921-4	—	- 13 ± 10.0	+ 106 ± 9.6	- 13 ± 5.9	- 19 ± 3.5	- 15 ± 2.8
871-80, 1901-10	—	+ 87 ± 10.0	+ 32 ± 9.4	- 42 ± 5.7	- 22 ± 3.5	- 14 ± 2.7
871-80, 1921-4	—	+ 14 ± 10.8	+ 75 ± 10.5	- 11 ± 6.5	- 17 ± 3.8	- 11 ± 2.9

(H. M. Woods, op. cit., p. 151.)

diately due, not to fewer attacks—judged by the relatively short period for which notification statistics are available, there has been but little change of incidence—but to less severity of attacks. The very reliable data of Goodall—compiled by one highly competent clinical epidemiologist, who observed the disease at the same hospital from 1895 to 1914—show that the more serious clinical forms have dwindled with the fatality. Why scarlet fever has become milder is not known. *Prima facie* one is apt to attribute the improvement to hospitalization. Sixty years ago the means of treating patients suffering from “fevers” were altogether inadequate; the general hospitals usually did not admit patients suffering from infectious diseases. The revelations made in a classical report prepared, at the instigation of Simon, by two clinicians, Dr. Bristow and Mr. Holmes, led to a movement for the provision of special hospitals. The original stimulus was not wholly, perhaps not even chiefly, a desire to prevent the spread of infection, but rather a desire to secure adequate medical care and nursing of very sick people. In course of time, however, although the need of good treatment was never forgotten or slighted, the preventive aspect of these hospitals acquired the most important place in the minds of administrators. In the great epidemic of influenza in 1918, when lives were lost because it was impossible to give adequate nursing and care to persons desperately ill, many people asked themselves whether the gain to public health from the side of prevention of infectious diseases justified one in reserving thousands of beds in public institutions for the reception of children suffering from so mild a disease as scarlet fever had become. The whole subject has been reviewed in the report of a Committee of Medical Officers of the Ministry of Health printed in 1927. The conclusion I should draw from the evidence is that the practice of twenty years ago could not be justified. The statistical evidence that isolation has had any sensible effect upon either the prevalence or the mortality of scarlet fever during the last twenty-five years is unconvincing. The fullest account of the subject is contained in Dr. H. M. Woods’ memoir.

The research was carried out practically on the same lines as that of Professor Karl Pearson and Dr. E. M. Elderton into the relations between diphtheria prevalence or mortality and hospitalization.

The data used were the experiences of forty-six English county boroughs and forty-eight English urban districts in the three quinquennia 1906-10, 1911-15, and 1919-23. To diminish the mere random fluctuation due to "small numbers," no districts were used unless in either 1906-10 or 1911-15 as many as ten deaths from scarlet fever had been registered within it. The primary averages are shown in Table 34.

TABLE 34  
SCARLET FEVER: MEAN AND STANDARD DEVIATIONS

Variables	1906-10		1911-15		1919-23	
	Mean	S.D.	Mean	S.D.	Mean	S.D.
Isolation rate per 100 cases ..	60.1	28.35	64.7	25.41	68.3	23.63
Case mortality per 1,000 cases	26.9	13.51	17.98	8.48	11.49	6.96
Death-rate per 100,000 population .. . . .	11.0	6.79	7.21	4.78	3.27	2.45
Attack-rate per 1,000 population	4.1	1.63	3.87	1.56	2.85	1.12

	Mean	S.D.
Overcrowding, 1911, per cent. .	8.49	8.07
Overcrowding, 1921, per cent. .	9.77	8.59
Infant mortality, 1911-15 ..	114.47	23.72
Infant mortality, 1919-23 ..	75.96	15.32

(H. M. Woods, *op. cit.*, p. 154.)

From the data the coefficients of correlation shown in Table 35 were computed.

It will be seen that the coefficients of correlation between isolation-rate and attack-rate are insignificant, that there is no general tendency for scarlet fever to be less prevalent in districts where the proportion of isolated cases tends to be above the average. Since these calculations involve the use of ratios having in some cases a common factor in each member of the correlated pair—for instance, if we correlated deaths per unit of population with cases per unit of population, we should be correlating two fractions with

TABLE 35  
COEFFICIENTS OF CORRELATION

Variables	1906-10	1911-15	1919-23
Isolation-rate and attack-rate .. {	-0.043 ± 0.069 + 0.427 ± 0.063	+ 0.049 ± 0.069 + 0.290 ± 0.069	-0.108 ± 0.069
Isolation-rate and death-rate .. {	-0.156 ± 0.068 + 0.153 ± 0.075	+ 0.010 ± 0.070 - 0.012 ± 0.075	+ 0.063 ± 0.069
Isolation-rate and death-rate (for constant attack-rate) .. {	-0.163 ± 0.068 - 0.204 ± 0.074	- 0.040 ± 0.069 - 0.305 ± 0.068	+ 0.159 ± 0.068
Isolation-rate and case mortality .. {	-0.290 ± 0.064 - 0.599 ± 0.057	- 0.194 ± 0.067 - 0.534 ± 0.054	+ 0.149 ± 0.068
Attack-rate and case mortality .. {	+ 0.063 ± 0.069 - 0.527 ± 0.056	+ 0.203 ± 0.067 - 0.495 ± 0.057	+ 0.095 ± 0.069
Attack-rate and death-rate .. {	+ 0.599 ± 0.045 + 0.677 ± 0.042	+ 0.749 ± 0.031 + 0.688 ± 0.040	+ 0.594 ± 0.045
Isolation-rate and case mortality (for constant number attacked) .. {	- 0.205 ± 0.064 - 0.474 ± 0.056	- 0.216 ± 0.066 - 0.512 ± 0.057	+ 0.153 ± 0.068

(H. M. Woods, op. cit., p. 154.)

a common denominator—the danger of what has been called “spurious” correlation arises. This can be eliminated (if it exists) by the method of partial correlation, and Dr. Woods found that the necessary further calculations did not modify the impression conveyed by the original results. That is a purely technical or formal difficulty. A material difficulty can be put as follows. The severity of any disease is a graded character which may or may not admit of quantitative definition, but a broad division is always possible between mild and severe. In the present mild type of scarlet fever—and all these calculations relate to a period within which scarlet fever has been very mild—the proportion of severe cases has been small, perhaps less than 10 per cent of the total. If in removal to hospital preference were given to the severe cases, then, in practically all districts, *all* the patients gravely ill would have gone to hospital, and consequently whether 15, 20, or more per cent of cases were isolated would be irrelevant so far as fatality were concerned. We should be applying our correlation method to material which could not give us any sensible answer. Thus, to go to an extreme, if all deaths occurred in hospital, in all districts, no arithmetical correlation between fatality- and isolation-rate could throw any light upon the clinical advantage of hospital treatment over domestic treatment, nor could the absence of any correlation be evidence that patients would have done as well at home.

It is certain that the proportion of the *deaths* which occur in hospital is greater than the proportion of *cases*, even in London with its great proportion of isolated cases. Thus in 1912 no less than 94 per cent of the deaths were in institutions, in the county boroughs 78 per cent, and in the urban districts 51 per cent. In 1919 (civilians) the percentages were: for London 93, for county boroughs 75, for urban districts 59. Even so, however, it is evident that (outside London) many of the deaths do not occur in isolation hospitals, while it is, to put it at the lowest, doubtful whether in fact severity of type of disease is a governing factor of admission where admission is selective; in the early stages prognosis cannot be confident. I think, therefore, that the failure to demonstrate significant correlation between indices of mortality or of prevalence and resort to isolation probably means what it seems to mean, viz. that there *is* no real relation. The same sug-

gestion is conveyed by such a Table as the next, which shows that, as between the two periods compared, areas with relatively little isolation have not improved less than those with relatively more isolation.

TABLE 36

	LONDON	COUNTY BOROUGHES AND URBAN DISTRICTS			
		Isolation-rate			
		Over 80 per Cent	70-80 per Cent	50-70 per Cent	Under 50 per Cent
Number of towns ..	..	(31)	(21)	(22)	(19)
Mean isolation-rate ..	1911-15 89.2	86.8	74.5	60.9	19.6
Attack-rate per 1,000 ..	3.47	3.81	3.98	3.98	4.04
Fatality-rate per 1,000 ..	15.1	17.9	16.4	17.7	19.2
Death-rate per 1,000 ..	5.3	7.2	7.7	7.1	7.2
Mean isolation-rate ..	1923-6 83.0	85.4	78.4	66.2	32.5
Increase or decrease, per cent .. .. .	- 7.0	- 1.6	+ 5.2	+ 8.7	+66.0
Attack-rate per 1,000 ..	2.5	2.7	2.7	3.0	2.7
Increase or decrease, per cent .. .. .	-28.0	-29.1	-32.2	-24.6	-32.2
Fatality-rate per 1,000 ..	9.4	12.3	10.9	12.3	9.6
Increase or decrease, per cent .. .. .	-37.7	-31.3	-33.5	-30.5	-50.0
Death-rate per 100,000 ..	2.39	3.43	3.06	3.55	3.02
Increase or decrease, per cent .. .. .	-54.6	-52.4	-60.3	-50.0	-58.0

(H. M. Woods, *op. cit.*, p. 158.)

Perhaps, however, it may be said that owing to unreliability of the data *no* correlations are likely to be significant. In fact, however, that is not the case. Thus it would be *a priori* probable that domestic overcrowding—whether *per se* or as an index of that poverty which is the mother of so many evils—should be positively correlated with mortality from such a disease as scarlet fever. Taking the measure of domestic overcrowding as the pro-

portion of the population in an area housed more than two persons to a room one finds the correlation of the death-rate with this index always positive. For the provincial towns the coefficients were  $0.195 \pm 0.067$  in 1906-10,  $0.283 \pm 0.064$  in 1911-15,  $0.250 \pm 0.065$  in 1919-23. In the boroughs of London for 1923-6 the coefficient was  $0.302 \pm 0.188$ . When the occupations of the male inhabitants of London were graded by the Registrar-General's method and the percentage of those falling into Classes I and II (the highest classes) taken as a measure, this time of prosperity, so that a negative sign of the coefficient of correlation is the equivalent of a positive sign in the previous trials, the coefficient proved to be  $-0.219 \pm 0.124$ .

Some of these values are small, having regard to the "probable errors," but they are consistent. They may well understate the stringency of association for a reason which I shall discuss here, although, of course, it is of general application and ought never to be forgotten when we use the method of correlation in public health work.

Most people nowadays are aware that the coefficient of correlation is not a satisfactory measure of the association of two variables when the law of increase of the mean value of one variable as the other increases (or decreases) is not approximately represented by a straight line, that is—to use a technical but fairly familiar term—when the regression is not linear. It is sometimes forgotten that, as our practical range of observation of social indices is very limited, particularly when, as in a case like this, we are working with aggregates, it is quite possible that, over the range of actual observation, the curve of regression may be approximately linear and horizontal, yet the variables by no means independent in the statistical universe. The Table on page 222 is an instructive example, which I quote from a paper by the late Dr. John Brownlee—one of the last and not the least valuable of the writings of that gifted investigator.

Obviously, if we had only had the data respecting housing of densities exceeding 1.5 persons per room—which might well have happened if the population had been so small that we were obliged to combine the lower density groups with that of 0.5, so largely swamping the former—we should have inferred that the environment (as measured) was not correlated with the fatality of enteric

fever at all. The inference would have been false. It would only have been fair to say that *over the range of our observations* no relation was demonstrable. It might well happen, as Brownlee remarked, that such variables as death-rate and density were connected by a relation of the form  $d = c \cdot D^n$ , where  $d$  is the measure of the death-rate,  $D$  that of the density, and  $c$  and  $n$  constants, the latter less than unity. As  $D$  increases,  $d$  will increase,

TABLE 37

TABLE SHOWING THE NUMBER OF CASES AND MORTALITY OF ENTERIC FEVER IN THE SANITARY DISTRICTS OF GLASGOW, GROUPED ACCORDING TO ROOM DENSITY, FOR THE YEARS 1898 TO 1902

Districts	Population, 1901	Room Density*	Enteric Fever		
			Cases	Deaths	Mortality, Per Cent
Group I .. ..	34,868	0.5 -1.0	106	10	9.4
Group II .. ..	83,255	1.0 -1.5	389	50	12.8
Group III .. ..	201,098	1.5 -2.0	1,308	217	15.8
Group IV .. ..	87,885	2.0 -2.25	711	116	16.3
Group V .. ..	237,161	2.25-2.5	1,743	296	16.9
Group VI .. ..	117,445	2.5 -2.75	1,003	164	16.3

\* Room density means the average number of persons per room.

(Taken from "On the Presence of Phenomena akin to Adsorption in Biology, as a Source of Fallacy in Statistical Inquiry," J. Brownlee, *Journal of Hygiene*, Vol. XXIII, 1925, p. 441.)

but at a slackening rate, until when  $D$  has passed beyond some particular value the values of  $d$  corresponding to increasing values of  $D$  will *seem* to lie upon a horizontal straight line. In biological language "life in an unhealthy environment for a certain range of density of population acts so as to depress the vitality, but there is a limit to the amount of injury which can take place" (Brownlee). That possibility should always be remembered when statistical analyses are performed—as they tend to be—either upon a limited class, inhabitants of "slums," or upon data so aggregated that extreme groups are merged in others. Applying the principle of this argument to the subject in hand, we are entitled to infer that for the scarlet fever of our generation isolation cannot be shown to have conferred any communal advantages in the way

either of prevention of infection or of reducing mortality. We have not the least justification for inferring that sixty years ago, when the ranges of severity of the disease and of domestic conditions were far wider than now, hospitalization was equally impotent. I do not know an uglier or more crippling fault in the statistical epidemiologist than to reason in such a way. It is almost, perhaps quite, as intellectually vicious as the *post hoc erga propter hoc* of the unstatistically minded.

NAWAB SALEH-UD-DIN

We have to deal with things as we find them. Our analysis of existing conditions is, as has been seen, incomplete, but far more searching than can be made of the epidemiological position fifty years ago. It is not for us to say that our fathers and grandfathers did the wrong thing epidemiologically speaking, that if public money had been spent differently we should have had at least as good a result as actually appears. But it *is*, I think, certainly our duty to face existing facts and to ask ourselves whether the recent method of using communal hospitals was justifiable. That, however, would carry me out of my province; it is a question of administration, of statesmanship which, as every Englishman knows, ought not to be meddled with by an expert, particularly that most malignant variety of expert the academic teacher.

It is within my province to point out that scarlet fever is the most beautiful example within the range of epidemiology—an even more striking example than that of smallpox—of change of type, a change which has been effected certainly twice and probably three times in this country within the limits of modern history. This has happened under wholly different environmental conditions. The change from malignancy to mildness occurred rather more than a century ago under conditions which were economically very unfavourable. The change fifty years ago progressed under certainly improving economic conditions. One can therefore hardly doubt that a factor has operated which, in the present state of knowledge, eludes our powers of definition. Once more *ignoramus*, but not, let us hope, *ignorabimus*.

The only recent outbreak of either scarlet fever or diphtheria which has been the subject of a special published official inquiry is that of the Ramsbury Rural District reported on by Dr. Hutchinson in 1923.\*

\* *Reports on Public Health Subjects*, No. 16.

Ramsbury is a Wilts village between Marlborough and the western boundary of the county of Berks, population 1,784. For many years before the inquiry there had been little scarlet fever or diphtheria in the rural district to which Ramsbury belongs. Between January 1, 1922, and January 15, 1923, there were 57 cases of scarlet fever, 19 of diphtheria, and 3 of both. In two instances there were 7 cases in one house, in one 6, in two 5, in one 4, and in four 3, in at least seven there were 2 (unfortunately no statistics of the numbers of children at risk).

A study of the house and time-incidence showed a correlation between the occurrence of further cases and the return of a patient from hospital. There were several houses in which cases of scarlet fever were followed after a brief interval by one or more cases of diphtheria; the interval was punctuated by the return to the family from Abingdon Isolation Hospital of a recovered case of scarlet fever. Diphtheria never occurred in a house with recent scarlet fever until a recovered case of scarlet had returned from the isolation hospital. In the borough of Abingdon at the relevant times 221 primary and 91 secondary cases of scarlet fever were notified, a high proportion of return cases, viz. 10 per cent, i.e. 22 cases of the total, occurred within 28 days of the return of a patient from hospital. In the rural district cases of diphtheria followed discharge of scarlet fever patients from isolation hospital.

The districts served by the hospital were not equally affected; the freedom of some was attributed by the medical officer of health to his practice of not sending patients suffering from scarlet fever into the hospital if they could be properly treated at home. The isolation hospital was found to be grossly overcrowded; it contained, when visited, one hundred and twenty patients in accommodation on the Ministry's standard (i.e. on the basis of 146 square feet per bed) for only forty-six. The conclusion was drawn that the isolation hospital was responsible for the spread of the disease.

#### RECOMMENDATIONS FOR FURTHER STUDY

Dr. Hilda M. Woods' report (Medical Research Council, Special Report Series, No. 180), supplemented by the papers cited therein,

provides a clear and detailed account of the subject so far as the experience of this country in the twentieth century is concerned. For earlier experience one must refer, as usual, to Creighton and Hirsch. Some of the older literature is cited in my report to the section of Hygiene and Preventive Medicine of the International Congress of Medicine which met in London in 1913, and is printed in its Transactions.

## VII

### SMALLPOX

SMALLPOX is epidemiologically one of the most interesting of diseases, and our means of information respecting its characters and history are enormous; the literature of the subject probably exceeds in bulk that devoted to all other epidemiological phenomena together. Unfortunately, for more than two hundred years—since the introduction into Western Europe of knowledge of inoculation—the literature has been tendentious. Anybody who writes on this—or indeed upon any other subject which has excited human passions—and fancies himself to be impartial is a self-deceiver. What I have to say *must* be tinged by personal bias; I *must* select and emphasize points which are congruent with my own system of thought and type of emotional reaction. Unfortunately, I can do little or nothing to help the reader to correct that bias; self-examination is a fallacious business at the best. I *think* that I am inclined to under-rate the value of personal experience when that experience is set out in the form of or accompanied by what seems to me bad statistical reasoning; I am *sure* that what—in modern jargon—is called an “inferiority complex” leads me to react violently, even when the verbal expression of the reaction may seem restrained, against official authority. Hence, *unpopular* opinions or the views of officially uninfluential minorities are probably stated by me with more emphasis, while orthodox views and evidence in support thereof are stated with less emphasis than a really unbiased judge would approve. The reader must try to guard himself against these errors and I am afraid it will be hard, for he can devote less time to study than it has been my duty to give. *Quis custodiet custodes ipsos?* is a question nobody has yet answered satisfactorily.

So far as the early epidemiological history of smallpox is concerned—its history down to the age of Jenner—I do not think any important error has been detected in the work of Charles Creighton; his estimate of the epidemiological importance of inoculation is less favourable than that of such contemporary writers as Jurin or Murray, but has not been effectively chal-

lenged. We may therefore take the historical facts to have been these. That the original home of smallpox was Africa, that it entered Europe with the Saracens, and was unknown in England before the Middle Ages. The first unequivocal record of smallpox in England is not earlier than the time of Henry VIII, and no good clinical account was available before 1561. By the time of James I smallpox was a malady to be reckoned with, and throughout the seventeenth century it was of considerable importance, and relatively of greatest importance as a killing disease to adults. In the eighteenth century smallpox was the reigning infectious disease and its incidence maximal upon children in the age group 0-5. This age distribution continued to be typical down to the third quarter of the nineteenth century, whereafter there was a transfer to older ages.

The only other observation I wish to make upon the earlier history is that physicians recognized the severity of epidemics to vary quite considerably, even in the period—say from 1660 to the end of the eighteenth century—when smallpox was a serious cause of mortality. Sydenham noted this, as can be seen if one compares his accounts of the regular and the irregular smallpox, and contrasted the epidemic constitution of the smallpox of 1667-9, when great numbers were attacked but relatively few died, with that of 1674-5. Almost a century later, J. A. Murray, of Göttingen, who published a curious history of smallpox and inoculation in Sweden,\* remarked upon the benignity of particular epidemics, instancing that of Stockholm in 1755—where most recovered without the help of medicine, the pustules dried up without rupture, and there was no swelling of the hands or face—and an outbreak in Gothenburg in 1760. Murray said this had occurred elsewhere, but was concerned to emphasize its exceptional character—it must, however, be said that he was a tentative writer, anxious to make the reader's flesh creep at the horrors of natural smallpox. I think, however, that there is little doubt that in the eighteenth century smallpox was, as a killing disease, quite of the force of scarlet fever in England in the early Victorian period. Perhaps there has been exaggeration as to frequency and severity of pock-marking and blindness. Still, there does not seem to me much to quarrel with in the

\* *Historia Inquisitionis Variolarum in Suecia, Gottingae, 1767.*

orthodox statement that smallpox was a deadly and loathsome disease.

A difficulty in giving an intelligible account of the epidemiological history of smallpox, over and above the fundamental one of bias, is the wealth of information; it is very hard to see the wood for the trees.

There is much to be said for Budd's view that it is easier to study the epidemiology of an illness (he was speaking of typhoid) in a sparsely populated area than in cities. I propose therefore first of all to give an account of the history of smallpox in the Commonwealth of Australia, availing myself of Dr. Cumpston's excellent monograph. I shall then examine the continuous record of the city of Baltimore, which Dr. Howard has worked out. These stories—although complex enough—are much less involved than the general history of our own country.

The history of Australia as a white man's country begins in 1788, and, although almost from the beginning there is a record of smallpox amongst the aboriginal inhabitants, the balance of evidence—a little doubtfully perhaps—inclines to the view that smallpox was really an imported complaint. As an epidemic sickness of whites, it is a modern disease in Australia. In the senior colony, New South Wales, no case has been recorded before 1831, while in Queensland no case was known before 1892.

The epidemiological history of smallpox in Australia therefore begins after vaccination had been recognized generally as a prophylactic measure. It appears from the statistics of births and vaccinations that some 30 per cent of those born in Australia in or after 1860 had been vaccinated, but that in Victoria much more resort had been had to this prophylaxis than in New South Wales. If we take the decennium 1871-80—that preceding the most serious outbreak recorded in Sydney—the total births were (New South Wales) 234,115, the recorded vaccinations 70,494, or 30·1 per cent. In the ten years before the Melbourne smallpox of 1884 there were 267,300 births and 217,153 vaccinations in Victoria, 81·2 per cent. Between 1850 and 1910 the history of smallpox in New South Wales has been as follows. In 1874 a single case of smallpox is known to have occurred at Newcastle. In December 1877 two patients with smallpox were successively landed from a steamship in Sydney harbour. These were the only

cases on the ship (which was released from quarantine on January 27, 1878). The first patient was landed on December 13th. On December 30th a case was discovered, that of a young woman living in a house next to the wharf where the steamer berthed; on January 11th two more cases, in two girls, were discovered; a little later the father, and, apparently, another sister of these girls were affected. On January 18th a case occurred on H.M.S. *Wolverine* at anchor in the harbour; there were three more on this vessel (contact between the first attacked sailor and the family just mentioned was asserted) and one upon another ship. In all there were twelve cases, and, apparently, four deaths. There was no extension through the city. In 1881-2 we come upon the largest pre-twentieth century outbreak; between May 23, 1881, and February 19, 1882, there were one hundred and fifty-four cases in Sydney. The first case is said to have occurred in the house of a Chinese, but no reliable statistics of the first period of the epidemic survive. It seems clear, however, that before September 2nd (after when more exact data were made available) seventeen streets or areas had cases, i.e. the disease was widely disseminated through the city and suburbs. After September 2nd more accurate data were compiled.

Table 38 (p. 230) gives certain particulars, of which the most interesting is the low ratio of cases to exposed to risk (the ratio of deaths to known cases was 25.9 per cent, which implies an ordinary severity). Very unfortunately, the vaccinal state of the exposed to risk is not known. It seems, however, clear that the presence in a populous city of a normally virulent strain of smallpox did not lead to any remarkable results in spite of the low level of crowd protection. Upon this presumption two comments are to be made. First, that the ratio of vaccinations to births is, self-evidently, a poor measure of the communal vaccinal state; second, that in the year itself a great deal of vaccination was done (more than 61,000 vaccinations are recorded in New South Wales in 1881).

In 1884, 5 cases of smallpox were discovered in the Orient Hotel, Lower George Street, Sydney; this was on August 3rd. From then to September 16th 14 patients were removed. Six weeks elapsed, and on October 25th another case was reported which led to a further series. In the first series of 14 patients, in addition to the original 5 (the disease had been in the house for a fortnight

TABLE 38  
SHOWING THE VARIOUS CENTRES OF SMALLPOX DURING THE EPIDEMIC

Locality or Street	Date of the First Appearance of Smallpox	Date of the Release of the Last House in the District	Number of Infected Houses	Number of Persons Living in these Infected Houses	Number of Cases of Smallpox
George and Cumberland Streets	May 25th	December 1st	5		4
Surrey Hills	June 14th	January 7th	6		7
Waterloo	June 16th	December 20th	3		7
Druitt Town	July 5th	August 27th	1		1
Glebe	July 7th	February 8th	5		6
Sussex Street and District	July 8th	January 3rd	20†		17
Ultimo	July 11th	December 30th	4		6
Woolloomooloo	July 14th	January 14th	10		7
Alexandria	August 1st	February 8th	3		4
Croydon	August 8th	September 8th	1		2
Darlington	August 10th	September 15th	1		2
Balmain	August 12th	September 22nd	1		3
Byrmont	August 12th	February 8th	14		11
Haymarket	August 16th	September 13th	1		2
Woollahra	August 29th	October 26th	1		2
McDonald Town	September 2nd	October 4th	1		1
Botany	September 4th	November 4th	1		2
Camperdown	September 5th	January 7th	2		2
Redfern	September 5th	January 14th	2		3
Pennant Hills	October 8th	December 1st	1		1
Burwood	November 5th	December 3rd	1		1
Liverpool Street	November 19th	February 2nd	4		7

\* These are Europeans, the number of Chinese in this district is not known.

† Two of these houses have no infection in them.

(Taken from *Smallpox in Australia*, by J. H. L. Cumpston, 1914, p. 14.)

and at first was taken to be chicken-pox), we remark that of 9, 2 were contacts and the remainder may have been in contact with the first batch. The next group consisted of 15 cases. Here again it was concluded that the infection had spread by contact. This story accounts for only 29 cases, but there seem to have been another 35 the official history of which is unknown. Again, therefore, we have a quite considerable number of cases in a populous city without serious spread. The deaths seem to have been 4, but in a table which accounts for 48 cases 8 are recorded as of confluent smallpox (6 in unvaccinated persons).

No other case is recorded until 1888. In this year a child aged 2 years is said to have died of confluent smallpox in a suburb of Sydney. Down to 1913 nothing which could be dignified by the name of an outbreak occurred.

We see then, in the course of more than a generation, ordinary smallpox in a community not, as would appear, having any high level of crowd immunity, introduced upon two occasions with sufficient effect to be followed by appreciable numbers of cases. Yet nothing of the nature of a serious epidemic followed.

The history of smallpox in Victoria is longer. In 1857—following the arrival of an infected ship—there were 16 cases with 4 deaths in Melbourne. In 1866 there were a few cases at Geelong. In 1868-9 there was another small outbreak in Melbourne and the vicinity; of 43 cases the first 27 were plausibly linked to the first case, that of the mate of a barque, but the others were not so easily accounted for. In 1872 a small outbreak occurred at Sandhurst near Bendigo; there were 10 cases, 3 fatal, all linked with a ship-borne patient. A few cases are recorded during the next twelve years, but the first and only prevalence of sensible magnitude was in 1884-5, when 56 cases (only 4 fatal) occurred in Melbourne. The origin of the outbreak was supposed officially at the time to be infection from a ship, but, as Dr. Cumpston points out, there are great difficulties in reconciling the chronology of the epidemic with this hypothesis, so that the possibility of a widespread internal distribution has to be considered. It was of course admitted that *Varicella* was widespread and there is room for doubt as to the diagnostic powers of some of the physicians concerned. Cases were distributed widely through the city and suburbs.

TABLE 39  
BALTIMORE: NUMBER OF DEATHS (D.) AND RATES PER 100,000 LIVING INHABITANTS FROM SMALLPOX (R.) FROM 1811 TO 1920 INCLUSIVE. VACCINATIONS AND VACCINATION RATES (R.), 1827-1918

Year	Smallpox		Year	Vaccinia		Smallpox		Vaccinia	
	D.	R.		Vaccinations	R.	D.	R.	Vaccinations	R.
1811	60	153	1866	—	—	13	5	2,076	835
1812	75	183	1867	—	—	—	—	891	350
1813	—	—	1868	—	—	—	—	2,216	851
1814	—	—	1869	—	—	—	—	1,822	684
1815	—	—	1870	—	—	—	—	1,329	487
1816	2	4	1871	—	—	—	—	5,364	1,023
1817	—	—	1872	—	—	1,043	366	50,650	17,756
1818	1	2	1873	—	—	469	161	87,739	30,084
1819	1	2	1874	—	—	—	—	1,136	381
1820	—	—	1875	—	—	1	—	1,741	571
1821	21	35	1876	—	—	—	—	1,634	525
1822	122	194	1877	—	—	—	—	3,397	1,068
1823	2	3	1878	—	—	1	—	1,457	449
1824	2	3	1879	—	—	1	—	2,186	659
1825	3	4	1880	—	—	1	—	8,467	2,501
1826	5	7	1881	—	—	11	3	20,100	5,816
1827	7	9	1882	4,019	5,251	551	156	94,693	26,850
1828	2	3	1883	—	—	633	176	217,050	60,319
1829	—	—	1884	2,762	3,474	1	—	1,567	427
1830	2	2	1885	—	—	—	—	2,012	537
1831	25	28	1886	3,308	3,824	1	—	3,042	797
1832	79	86	1887	673	730	—	—	4,066	1,045
1833	32	34	1888	—	—	—	—	7,458	1,778
1834	71	72	1889	1,068	1,080	—	—	7,411	1,735

1835	3	—	—	—	1800	—	—	—	11,281	2,596
1836	1	130	123	1891	1891	—	—	—	10,703	2,421
1837	53	2,753	2,512	1892	1892	—	—	—	33,249	7,398
1838	72	1,000	882	1893	1893	—	—	—	20,875	4,570
1839	2	2,213	1,889	1894	1894	—	—	—	42,042	9,059
1840	11	—	—	1895	1895	—	—	—	12,990	2,755
1841	1	—	—	1896	1896	—	—	—	13,759	2,875
1842	1	2,655	2,058	1897	1897	—	—	—	12,905	2,656
1843	—	2,254	1,694	1898	1898	—	—	—	11,817	2,397
1844	—	—	—	1899	1899	—	1	—	36,491	7,296
1845	110	3,367	2,379	1900	1900	—	—	—	9,023	1,780
1846	115	3,707	2,542	1901	1901	—	—	—	15,400	2,997
1847	2	1,805	1,201	1902	1902	—	7	1	46,412	8,913
1848	5	1,763	1,139	1903	1903	—	2	—	11,566	2,193
1849	20	2,159	1,355	1904	1904	—	4	1	23,440	4,389
1850	153	1,987	1,212	1905	1905	—	—	—	5,979	1,106
1851	104	3,738	2,217	1906	1906	—	—	—	9,319	1,703
1852	66	1,948	1,123	1907	1907	—	—	—	3,769	681
1853	9	1,604	900	1908	1908	—	—	—	5,926	1,058
1854	26	2,513	1,371	1909	1909	—	—	—	1,277	1,226
1855	50	3,910	2,077	1910	1910	—	—	—	8,161	1,426
1856	8	2,236	1,156	1911	1911	—	—	—	7,561	1,307
1857	91	4,121	2,076	1912	1912	—	—	—	4,663	798
1858	310	8,576	4,209	1913	1913	—	—	—	27,424	4,648
1859	1	1,770	847	1914	1914	—	3	1	15,693	2,634
1860	—	2,277	1,062	1915	1915	—	—	—	7,223	1,201
1861	1	2,992	1,360	1916	1916	—	—	—	6,515	1,073
1862	34	1,663	737	1917	1917	—	—	—	8,894	1,452
1863	252	2,862	1,238	1918	1918	—	—	—	10,230	1,656
1864	436	6,044	2,552	1919	1919	—	—	—	—	—
1865	18	2,315	954	1920	1920	—	—	—	—	—

(Taken from *Public Health Administration, etc., in Baltimore, 1797-1920*, by W. T. Howard, Table 34, pp. 278-9.)

Victoria had no real smallpox experience from then until 1921, when two cases were reported in Melbourne and five in Geelong. The Melbourne cases were of the ordinary type (one of the patients

TABLE 40

MORBIDITY BY MONTHS AND YEARS AND THE MONTHLY ANNUAL AND SMALLPOX FROM 1899

C. = cases.

Year	January		February		March		April		May		June		July		August	
	C.	R.	C.	R.	C.	R.	C.	R.	C.	R.	C.	R.	C.	R.	C.	R.
1899	2	5	2	5	7	16	2	5	3	7	—	—	1	2	—	—
1900	—	—	—	—	—	—	9	22	2	5	3	7	1	2	1	2
1901	3	7	1	3	4	9	2	2	2	5	1	2	—	—	—	—
1902	—	—	14	35	3	7	3	7	5	11	—	—	1	2	—	—
1903	2	4	6	15	10	22	5	12	13	29	1	2	1	2	—	—
1904	1	2	4	10	9	20	14	32	20	44	10	23	—	—	—	—
1905	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
1906	14	30	19	45	14	30	9	20	2	4	—	—	—	—	—	—
1907	—	—	2	5	—	—	—	—	—	—	1	2	—	—	—	—
1908	1	2	2	5	—	—	1	2	1	2	—	—	1	2	—	—
1909	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
1910	—	—	—	—	1	2	1	2	—	—	—	—	—	—	—	—
1911	—	—	—	—	1	2	—	—	—	—	—	—	—	—	—	—
1912	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
1913	27	54	13	287	1	2	—	—	2	4	1	2	2	4	—	—
1914	29	57	82	179	143	283	44	90	15	30	11	22	1	2	—	—
1915	—	—	—	—	12	23	—	—	—	—	—	—	—	—	—	—
1917	—	—	2	4	7	13	3	6	—	—	—	—	—	—	—	—
1918	7	13	5	11	10	19	10	20	9	17	5	10	—	—	—	—
1919	—	—	1	2	9	15	4	7	3	5	—	—	1	2	—	—
1920	4	6	5	9	2	3	10	17	6	10	4	7	1	2	2	3

\* Those years in which cases did not  
(W. T. Howard,

died), but those at Geelong were said (in spite of the fact that one of the patients died in confluent smallpox) to be of the mild or "alastrim" type of infection which prevailed in 1913-14.

We have seen that for more than a quarter of a century down to 1913, smallpox was without epidemiological importance in New South Wales. In May 1913 a new epoch began with the appearance

of an unusual rash amongst the staff of a manufactory of under-clothing in Sydney; this was recognized as smallpox, and it extended to no less than twenty-eight country towns and districts, so

TABLE 40 (continued)

ANNUAL RATES OF MORBIDITY PER 100,000 LIVING INHABITANTS FROM  
TO 1920, INCLUSIVE\*

R. = rate.

Year	Sep-tember		October		Novem-ber		Decem-ber		Total			Per Cent Case Fatality	
	C.	R.	C.	R.	C.	R.	C.	R.	C.	R.	Average Rate of Morbidity by 5-year Periods	Annual	Average by 5-year Periods
1899	—	—	—	—	—	—	1	2	18	4	—	6	—
1900	—	—	—	—	—	—	1	2	17	3	2	—	1
1901	—	—	—	—	1	2	1	2	14	3	—	—	—
1902	2	5	—	—	—	—	1	2	29	6	—	24	—
1903	1	2	1	2	—	—	1	2	41	8	—	5	—
1904	—	—	—	—	—	—	—	—	58	11	—	7	—
1905	—	—	—	—	3	7	19	41	22	4	6	—	7
1906	—	—	—	—	—	—	—	—	58	11	—	—	—
1907	—	—	—	—	—	—	1	2	4	1	—	—	—
1908	—	—	—	—	—	—	—	—	6	1	—	—	—
1909	—	—	—	—	—	—	2	4	2	—	—	—	—
1910	—	—	—	—	—	—	—	—	2	—	3	—	—
1911	—	—	—	—	—	—	—	—	1	—	—	—	—
1912	—	—	—	—	4	8	11	22	15	3	—	—	—
1913	3	6	—	—	—	—	1	2	50	8	—	—	—
1914	—	—	—	—	—	—	—	—	325	55	—	1	—
1915	—	—	—	—	—	—	—	—	12	2	14	—	—
1917	—	—	—	—	1	2	10	19	23	38	—	—	—
1918	—	—	—	—	—	—	—	—	46	7	—	—	—
1919	—	—	—	—	—	—	—	—	18	3	—	—	—
1920	—	—	—	—	—	—	—	—	34	5	10	—	—

occur have been omitted from this Table.

op. cit.)

that in the year 1,073 cases were recognized in the State (1,017 in Sydney); in 1914, 445 cases were found in the metropolis and 183 in other areas. In 1915 there were 41 cases in Sydney and 430 elsewhere; in 1916, 16 in Sydney, 92 elsewhere; in 1917, none in Sydney, 119 elsewhere. This considerable prevalence differed essentially from any previous experience, although in one respect

the difference was rather of degree than kind. As we have no knowledge of the vaccinal state of the exposed to risk, inferences must be hazardous, but the enormous disproportion of unvaccinated to vaccinated amongst the attacked (of 1,037 patients treated at the Sydney Quarantine Station in the six months ending January 31, 1914, only 53 had been vaccinated) suggests that the advantage of the vaccinated was greater in respect of attack-rate than in earlier "classical" experience. In respect of fatality the change was enormous. The Australian experience teaches us two lessons. The first is that in an imperfectly protected community "classical" smallpox does not necessarily spread widely; for it to become epidemic there is required a *tertium quid*. The second is that within such a community a form of smallpox which differs notably from the classical type may become widespread.

Let us now examine the history of a crowd very different from the Australian. There we had indeed—in the instances of Sydney and Melbourne—dense urban aggregations, but the means of entrance of infection were narrowly restricted; they were virtually limited to importation from overseas, so that the position was very different from that of a city situated within a well-populated land area. A good example of a crowd of the latter type is the city of Baltimore, the epidemiological history of which has been written by Dr. William Travis Howard in a most interesting volume.

The fundamental statistical data are set out in Tables 39 and 40.

With respect to immunization, it would seem from the text that during the first twenty years covered by the Table, although figures are not available, a good deal of vaccination was done, but that at the end of it not more than half the population were vaccinated. Epidemiologically, 1811-30 is a period of quiescence, interrupted by two severe epidemics some ten years apart—a record not unlike those of pre-vaccination days. From 1831 to 1866 the picture is different; very few years passed without deaths from smallpox, and twice (once during the Civil War) there were epidemics of the order of severity of those of 1811-12 and 1821. It is clear that a good deal of vaccination was done, equally clear that not only was the enforcement of this method of protection very lax, but that the control of movement of persons suffering from smallpox was inefficient. In 1864 greater powers were conferred upon the health authorities and a measure of

compulsory vaccination of infants passed by the legislature. Between 1866 and 1872 there were no recorded deaths from smallpox, but at the end of 1871 the worst outbreak in the history of the city began and caused more than 1,500 deaths (when deaths

TABLE 41

MONTHLY MORBIDITY AND MORTALITY, AND RESPECTIVE RATES PER 100,000 LIVING INHABITANTS FROM SMALLPOX DURING THE EPIDEMIC 1882-3

C. = cases. D. = death. R. = rate.

	1882				1883			
	C.	R.	D.	R.	C.	R.	D.	R.
January .. ..	46	154	2	7	1,259	4,119	329	1,076
February .. ..	53	196	6	22	542	1,964	194	703
March .. ..	38	127	10	33	175	573	65	213
April .. ..	78	269	12	41	92	311	28	95
May .. ..	107	357	17	57	35	115	12	39
June .. ..	106	366	13	45	9	30	4	14
July .. ..	114	381	22	73	2	7	1	3
August .. ..	237	791	24	80	—	—	—	—
September .. ..	255	880	71	245	—	—	—	—
October .. ..	362	1,209	63	210	—	—	—	—
November .. ..	483	1,666	94	324	—	—	—	—
December .. ..	946	3,158	217	724	—	—	—	—
Total .. ..	2,825	801	551	156	2,114	587	633	176

(W. T. Howard, op. cit.)

in the Marine Hospital are added the total exceeds 2,000). During the course of this prevalence many vaccinations were done, and at its end almost all the inhabitants had either had smallpox or been vaccinated. During the next six years, Baltimore was practically free from smallpox, but towards the end of 1881 a new serious prevalence began; there were some 5,000 cases and nearly 1,200 deaths.

"Through the thirteen months from January 1882, the disease grew in incidence and in fatality in steady and almost uninterrupted progression, apparently uninfluenced by season or by vaccination" (see Table 41). Throughout this prevalence vaccination was resorted to so freely that it is estimated between 85 and 90 per cent of the

population had been submitted to apparently successful vaccination. Dr. Howard gives some calculations leading to the conclusion that the attack-rate upon the previously unvaccinated was rather less than twice and the fatality almost four times that of the vaccinated. Differences of this order have usually been recorded; their *prima facie* interpretation has been hotly contested, not, in my opinion, with logical success. Since then we hear no more of smallpox as a killing disease in the city of Baltimore, but we still hear of prevalences; in 1914 there were as many as three hundred and twenty-five notified cases (with but three deaths). Dr. Howard's commentary upon this story I shall quote almost in full.

"The history of smallpox in Baltimore presents some striking features from which may be drawn instructive information in regard to the natural history of the disease and valuable lessons in public health administration. The first concerns the endemic and epidemic states of the disease in the community. While it is true that, unlike other members of the group, from the earliest times its natural course has been modified by artificial interferences with its entrance and spread in the city, enough is known of the value of these at different periods to allow for their discount with some measure of certainty. Between 1800 and 1830, when the use of inoculation and of vaccination was comparatively restricted, and quarantine and general methods designed to prevent its spread among the inhabitants were of the most meagre sort, the disease occurred repeatedly in small and twice in large outbreaks without becoming endemically established. On the other hand, between 1831 and 1866, in association with much wider use of vaccination and of restrictive measures of a general sort, smallpox was very commonly, if not constantly, endemic. During this period upon this endemic state there were imposed a number of periodic epidemic waves, which were not usually associated with mortality-rates as high for individual years as were those experienced before and later. Between 1867 and 1883 this phase was succeeded by a return to the conditions prevailing before 1830, when the disease was no longer endemically established, but appeared only from time to time, with two very serious epidemics (1872-3 and 1882-3) separated by an interval of ten years.

"These two epidemic visitations, with mortality-rates, when proper allowances for deaths occurring at the smallpox hospital are made, much higher than ever before experienced, occurred after a period of increased public vaccination-rates, the establishment of a State vaccine institution for the propagation of a potent virus, the passage of State laws requiring compulsory vaccination of infants, and the exclusion of unvaccinated children from school. As neither of these legal provisions was systematically obeyed (the commissioner of health discarded the State virus as impotent in 1872), any effects which would in theory be credited to

them must be largely discounted in practice. However, in spite of these activities as planned and executed, and of the most active and widespread vaccination campaigns ever conducted in the city, these two epidemics lasted for the usual period of eighteen or twenty months, and, relative to the population, were even severer in degree than any of their predecessors.

"Since 1884 smallpox has taken on a new phase, one which is without parallel in previous experience. Though introduced many times, and since 1897 present each year, the disease has not acquired endemic status and has only twice (1902-4 and 1912-14) threatened to become seriously epidemic. While, owing to the fact that most of those ill of the disease have of late years been removed to quarantine hospitals without the city, the deaths officially credited to smallpox by no means represent the actual fatality; nevertheless, the number has been small, and in comparison with earlier periods almost negligible. During this period vaccination has increased, virus has been greatly improved, and case-reporting and isolation have been secured. Another factor of considerable importance is that since 1884 the bulk of the European immigration has come from countries where vaccination was enforced, while previous to this date the contrary was the case. Since 1900, at least, the disease has been introduced almost entirely by negroes from the South, and has been largely confined to this race.

"It is of considerable interest that severe epidemic outbreaks have tended to occur at about ten-year intervals, falling at or near the beginning of decennia, as in 1811, 1821, 1831, 1850, 1862, 1872, 1882, 1902, and 1912.

"It seems clear that until 1884 the prevalence and mortality of smallpox were governed to a much greater degree by its inherent natural characteristics in their relation to the population than by any artificial interferences, including vaccination, that were interposed. It appears that before 1900 the course of the disease could have been only modified and not controlled by vaccination as practised."

In my opinion this is the conclusion to which the historical facts must lead one.

Some light, though not very much, is thrown upon the question by an examination of the statistics of deaths from smallpox in London since the end of the seventeenth century. One may say that before the third decade of the nineteenth century smallpox in London was an uncontrolled disease, for it is doubtful whether the resort to inoculation was ever upon a sufficient scale to possess statistical importance. If we compare the evolution in time of smallpox prevalences before and after the introduction of vaccination, is there a difference of form? In the old days did an epidemic flare up and pass through its stages of rise, decline, and

fall more quickly than in the nineteenth century? An attentive study of the records does not enable me to say "Yes." I do not think that, by statistical analysis, a generic difference of epidemic form can be established, but the subject is too difficult and not of sufficient intrinsic importance to be discussed at length here.

There is, however, no doubt at all that in one respect the epidemiology of eighteenth-century smallpox differed materially from that of the last fifty years of the nineteenth century, viz. in age distribution.

In the eighteenth century and still in the first half of the nineteenth smallpox was mainly a disease of children; as recently as 1851-60 the rate of mortality in no age group later than 5-10 amounted to one-fifth the rate in the age group 0-5, and the mortality at 5-10 was one-quarter the mortality at 0-5. In the epidemic of 1871-2 the relative predominance of the first age group was considerably lessened; the mortality at 5-10 was half that of 0-5, at 10-15, 18 per cent; 15-25, 32 per cent; 25-35, 30 per cent; 35-45, 19 per cent; 45-55, 12 per cent, and at ages over 55, 5 per cent of the mortality of infancy. Creighton thought that this was largely due to the ravages of other zymotics, especially scarlet fever, at the epoch of the great epidemic, but he went rather further, writing:

"It would be a not incorrect summary of the incidence of smallpox in Britain to say that it first left the richer classes, then it left the villages, then it left the provincial towns to centre itself in the capital; at the same time it was leaving the age of infancy and childhood. Of course it did none of these things absolutely; but the movement in any one of these directions has been as obvious as in any other. Measles and scarlatina have not shown the same tendency to change or limit their incidence. Smallpox may have surprises in store for us; but, as it is an exotic infection, its peculiar behaviour may not unreasonably be taken to mean that it is dying out—dying, as in the death of some individuals, gradually from the extremities to the heart."

So far as the age distribution is concerned, the data of the last large-scale prevalence of the classical type, that of 1901-2, followed the rule with a partial exception; the rate of mortality at 5-10 was a smaller fraction of that at 0-5 than in 1871-2, viz. 31 instead of 50 per cent, but at all later ages the rates, in terms of that at 0-5, were higher: 79 per cent at 25-30, 80 per cent at 35-45, 52 per cent at 45-55, and 24 per cent at later ages. A possible

contributory factor might be that the proportion of adults protected by prior attack was higher in the adult generation of 1871-2 than in that of 1901-2, but I do not think there is much evidence that this was an important factor. Creighton's explanation of the relative immunity of the infants by a prior weeding out will hardly meet the case. By 1900 the importance of scarlet fever had already diminished to a shadow of its mid-Victorian importance, and its place had not been taken by any other great destructive agent.

Creighton was not, of course, willing to admit that vaccination was part of the explanation. But if we hold, as I certainly do, that vaccination does confer a substantial measure of personal immunity which decreases with time, and agree—as we clearly must—that a much larger proportion of young children than of adults in the population exposed to risk at any moment during the last fifty years had been recently vaccinated, it would be perverse to refuse to entertain the hypothesis that the modification of the age distribution has been in part due to vaccination. Naturally the whole cogency of the argument depends upon acceptance of vaccination as being really an immunizing process. The reader will also observe that I do not claim the whole of this change for vaccination because, as I pointed out in the chapter on "Scarlet Fever," a somewhat similar change has taken place in the age distribution of scarlet fever.

I have now traced the epidemiological history of the classical smallpox of our textbooks down to our own time. It remains to speak briefly of a very remarkable phenomenon which has called into existence a literature already large and steadily growing, viz. the emergence of a variety of smallpox which, while in many of its clinical features identical with the smallpox we have been considering, differs in that the mortality it causes is negligibly small.

I have said that long ago mild epidemics of smallpox were reported, and whether all pre-nineteenth century outbreaks of varicella—first, I think, clinically differentiated from smallpox by the elder Heberden—would have been distinguished by modern epidemiologists from *alastrim* is a subject which a clinical epidemiologist with historical tastes might profitably investigate. This, however, is certain, that it is only within the last quarter

of a century that widespread outbreaks of an infectious disease differing only from "classical" smallpox in one particular—certainly the most important particular—viz. an almost negligible fatality, have been reported.

The outbreak in Brazil reported on in 1910 by Ribas and said to have led to a quarter of a million cases was not the first—in South Africa a similar phenomenon dates back to 1895—but the first to excite much attention. To that outbreak we owe the name "alastrim" (a Brazilian derivative of a Portuguese verb, *alastrar*, which conveys the idea of something which melts and spreads). Within a few years reports multiplied; one hears of the South African focus, the West Indian focus, the outbreaks in Australia, and the prevalences in England thanks to which we were, statistically speaking, the most smallpox-ridden land of West Europe from 1921 to 1933. In England, excepting a small outbreak in Cambridge in 1902, smallpox was of the "classical" type until after the war. Then in 1919 a localized epidemic of smallpox in Suffolk and Norfolk was characterized by a dissociation of fatality from superficial clinical signs, and thereafter the annual total of notifications rose until it was normal to record thousands of cases yearly of an essentially benign disease.

It always happens in medicine that when a clinical or epidemiological phenomenon emerges which is not within the personal experience of those who see it, some acclaim it as a "new disease" while others retire into libraries, and, having discovered more or less apposite passages in the works of the illustrious defunct, reprove their unlettered colleagues for culpable ignorance of medical classics. Although I am not distinctly aware that anybody has yet stated that the illustrious Sydenham saw cases of *alastrim* every day of his life, the reader of Professor Ricardo Jorge's excellent history of the controversy can satisfy himself that all possible and some impossible positions have been occupied by epidemiologists and public health officers of repute. The controversy—like all controversies having even a remote connection with the terrible subject of vaccination—has been carried on with more heat than light. With this discussion, which in my opinion differs from scholastic discussions of the fifteenth and early sixteenth century only in as much as the modern disputants are much less expert in formal logic, and pay themselves and one

another in much baser verbal coin than did St. Thomas Aquinas and his abler students, I shall not trouble the reader at all.

I have probably wearied the reader sufficiently in my earlier chapters by insistence upon the distinction between the epidemiological and other points of view. Epidemiologically considered, the present type of smallpox differs from the "classical" type no more than the scarlet fever of our day differs from that of fifty years ago, and I see no scientific profit in discussing whether it is more convenient to speak of it as alastrim, parasmallpox, variola minor, or just plain smallpox. The fundamental epidemiological fact is that the type has changed, and the process of change has not in its time-sequence differed very much from that which affected scarlet fever in the nineteenth century. Where it has differed from that classical instance is that the method of spread of the mild prevalent form throughout England is consistent with the hypothesis that we are dealing with an exotic. That is the reason why sensible men do differ on practical issues. If we could be sure—as we can reasonably be with respect to scarlet fever—that we are merely witnessing an internal evolution of epidemiological species, we should have little anxiety. We should be able cheerfully to abandon vaccination, and should feel that we were not really running any grave risk because a reversion to the previous type might be expected to take time. But we are *not* sure of this. Suppose that this variant were introduced from without, that in view of its benignity even the pretence of compulsory vaccination were abandoned, and that sooner or later the genuine Simon Pure, the "classical" smallpox, returned, what would be the price to be paid?

I do not think that a logically satisfactory answer to that question can be given. My own opinion is that Dr. Killick Millard's policy is the right one and that the risk of a sudden reversion to the older type of smallpox is a small one. Provided that we keep our powder dry, that we have always available a completely sufficient supply of potent lymph, I think we may view the passing of even nominally compulsory vaccination with equanimity. Although the time is past when it would have been *de rigueur* for an academic teacher to make a formal profession of faith in the efficacy of vaccination against smallpox, I have no objection to saying that, in my opinion, the orthodox view that vaccination

is a very effective safeguard against the risk of dying from small-pox if acquired, and a powerful safeguard against taking the disease if exposed to risk, is quite correct. I differ from both the orthodox and the heterodox in my estimate of the character of Edward Jenner. The epidemiological importance of that particular controversy is insignificant, and if we were the "scientists" of fiction, swayed only by reason, it would be a pure waste of valuable time to discuss the rights and wrongs of Edward Jenner. Actually we are human beings, and it will be many years before Jenner's life ceases to be used to point a moral and adorn a tale—indeed, to point several morals and adorn contradictory tales. Therefore I shall give Jenner's life more space than my scientific conscience can justify.

#### RECOMMENDATIONS FOR FURTHER STUDY

In addition to the works cited in the text, Hirsch's chapter should be consulted

## VIII

### EDWARD JENNER AND CHARLES CREIGHTON

IN 1923 the centenary of Edward Jenner's death was celebrated. Eminent physicians made speeches, and it was a source of satisfaction to one of them to be able to say that his father had been vaccinated by Jenner himself. No jarring note was struck; opponents of vaccination were only referred to with that vague if energetic abhorrence which, in a pious congregation, is the portion of "infidels" or "atheists." Four years later there died in a Northamptonshire village an energetic old gentleman, known to his humble neighbours by numerous acts of kindness, who may have derived from the oratory of 1923 a certain bitter amusement, because—he was the most widely read "doctor" of his time—he would have recollected that the festal orators of 1923 were the veriest cynics in comparison with a medical official of 1857, afterwards the famous Sir John Simon, who wrote: "Among the dairy-folk of Gloucestershire there was a curious tradition . . . that persons who had suffered from this cowpox, as it was called, were by it rendered insusceptible of smallpox. Words to this effect were once spoken in the hearing of Edward Jenner, then a village doctor's apprentice in the neighbourhood of Bristol. They were never afterwards absent from his mind. Thirty years elapsed before their fruit was borne to the public; but incessantly he thought and watched and experimented on the subject; and the work in which at length he recorded the incomparable results of his labour may well have commanded the confidence of reflecting persons. Little would ever be heard of objections to vaccination if all who undertake the responsibility of its performance, and all who feel disposed to resist its adoption, would but thoroughly study that masterpiece of medical induction, and imitate the patience and caution and modesty with which Jenner laid the foundation of every statement he advanced."\*

It may even be that it was Simon's apotheosis of Jenner as the Ideal Philosopher which provoked Charles Creighton to tell, forty-three years ago, what he thought was the whole truth about

\* Simon, *Public Health Reports*, Vol. I, p. 184.

Edward Jenner. Perhaps Creighton did not wholly succeed in this attempt; perhaps Jenner the Complete Rogue of Creighton is as much an exercise in mythology as Jenner the Ideal Researcher of Simon. Certainly, in 1935, the character of Jenner is of about as much practical importance as the character of Tiberius Caesar. No more orations will be needed for fourteen years, and on the bicentenary of Edward Jenner's birth I have no doubt Simon (the writer from whom Simon cribbed—Baron—is too long winded to be used by public speakers), not Creighton, will provide the material. But some of my readers will be asked by members of Public Health Committees what they think of Jenner, and it will be as well for them to be familiar with his story.

Edward Jenner was born on May 16, 1749, the son of a country parson, and at the age of thirteen was apprenticed to a firm of what we should call general practitioners of medicine. In our time, whether a lad aspires to the glory of becoming a "well-known Harley Street physician" or is content with the hope of family practice in the country, his undergraduate training will be the same. Now there is nothing in law or ethics to prevent a man practising as a "physician" in Harley Street and a general practitioner in Hampstead. In the eighteenth century the separation was absolute. It was no more practicable to combine the characters of physician, complete with gold-headed cane, and of apothecary than it would be now for a barrister lacking briefs to practise as a solicitor. In Jenner's time, the only way to become a general practitioner was by serving articles of apprenticeship as an embryo solicitor must now (unlike the latter, the doctor's apprentice, in Jenner's day, had no examination to pass). The apprentice was bound "to serve in and be taught the Arts mysteries or Profession of a Surgeon Apothecary and Accoucheur" (I am quoting from my grandfather's indentures made in 1844, but no doubt following ancient precedents) and the master undertook to "teach and instruct or cause to be taught and instructed" the pupil "in the Arts, Mysteries, Business, or Professions of a Surgeon Apothecary and Accoucheur." It was no more necessary in the eighteenth century for the pupil to attend lectures or pass examinations than it was necessary for a carpenter's or blacksmith's apprentice to do so. An apothecary must, of course, have had more general education than a carpenter, and it was not impossible

for him in later life to become a "physician." His easiest course (that followed in due time by Jenner himself) would be to obtain the degree of M.D. from the University of St. Andrews, which in the eighteenth century seems to have granted its doctorate on easy terms, perhaps not unlike those of joining a learned society, but if he desired to practise in London he would have to obtain (by examination) the licence of the College of Physicians.

If, however, a young man wished to be a "physician" from the beginning, he would certainly have to attend lectures and pass examinations. The examinations might have been, like the lectures, on theoretical rather than practical matters, but it was not possible to become a College Physician without being, in the eighteenth-century sense, an educated man. In that sense a country apothecary had no need to be an educated man at all. Mr. Chillip in *David Copperfield* was socially and educationally much nearer the village chemist of our time (educationally, a good deal behind him) than the modern general practitioner. Jenner's general culture was that of Mr. Chillip, not that of Dr. Parker Peps. But in one extremely important respect Jenner had a better education than either Mr. Chillip or Dr. Parker Peps. He was a resident pupil with John Hunter for two years. John Hunter, as everybody knows, was one of the greatest British men of science, one of the founders of experimental pathology and biology. Hunter's general culture was no wider than that of Jenner; he could not have swopped Greek and Latin quotations with Sir George Baker, and he jeered at the Universities of Oxford and Cambridge, but he was a great investigator who did not suffer fools gladly, and the fact that he liked young Jenner and corresponded with him almost to the day of his death (in 1793) is a better testimonial of Jenner's ability than any of Baron's myths. Hunter's letters are extant; with their help and that of the less miraculous of Baron's stories there is no difficulty in realizing the Jenner of the years from 1772 when he began practice as a surgeon apothecary to 1789 when he was elected a Fellow of the Royal Society. The picture is that of a reasonably prosperous country practitioner, a likable clubbable fellow, who could sing a good song and turn a copy of verses, *with* a taste for natural-historical observation and speculation. It was the turn for natural history which formed the bond with Hunter and the tendency to rather vague speculation which

incurred the famous admonition—"But why do you ask me a question by the way of solving it? I think your solution is just, but why think? Why not try the experiment?" Jenner was only twenty-six when he received that friendly hint. Jenner's output of experiments and observations was meagre, although Hunter incessantly urged him to make observations on the winter temperature of hedgehogs. "The sole outcome of all this dunning year after year," writes Creighton, "was the brief record of four temperature observations made by Jenner on a hedgehog (two in winter one in summer, and one at a season not stated), which Hunter introduced in half a dozen lines into his paper on 'Animal Heat' when he reprinted it in 1786." Of medical papers there is a note on a method of preparing tartar emetic and an observation on calcification of the coronary arteries. Over this period our rival mythologists, Baron, Simon, and Creighton, have exercised their gifts: the two former exaggerating the intrinsic importance of what little Jenner really published but always keeping the centre of the stage for the grimly self-denying thinker brooding over the words he heard as a boy about immunity to smallpox and so unable to give much attention to other things; the last named steadily emphasizing the trifling character of Jenner's known achievements. It was psychologically inevitable that this should be; we cannot even hope to find truth unless we realize the natural biases of the rival mythologists. Baron was an intimate friend of Jenner, Simon was a public health propagandist and administrator and an opportunist. Neither of them was an exact scholar, and only Simon had any knowledge at all of scientific investigation. Both of them were convinced that cowpox inoculation had proved an immensely important measure of prophylaxis. Creighton was an exact scholar, a highly educated man, and quite as honestly convinced of the contrary. Creighton, although he did do in fact a good deal more work in a laboratory than Simon had ever done, was essentially a scholar in the bookish sense, with the admirable qualities and the defects of that kind of person. He was also a logical Scot, and out of sympathy with unsystematic-minded people. Simon, on the other hand, was practical-minded up to or even a little beyond the verge of intellectual honesty; he could understand that important truths might be reached in very unacademic ways. Creighton could not. In the next stage

of our hero's career, we shall find not the admiring Boswell but the erudite historian going hopelessly astray. We have come to the episode of the cuckoo.

In the early days of the Hunter-Jenner correspondence the subject of the cuckoo cropped up in 1773; but it is not until 1786 that Jenner actually produced a manuscript, and in this there was no reference at all to the dramatic ejection from the foster-mother's nest of her own offspring, not by herself, but by the young cuckoo. On June 19, 1787, Jenner claimed to have seen a newly hatched cuckoo actually pitching a newly hatched hedge sparrow out of the nest. He asked for the return of his manuscript, recorded this and other observations, including one to the effect that there is a peculiar depression in the back of the young cuckoo which "seems formed by nature for the design of giving a more secure lodgment to the egg of the hedge sparrow or its young one when the young cuckoo is employed in removing either of them from its nest. When it is about twelve days old this cavity is quite filled up, and then the back assumes the shape of nestling birds in general."

This revised paper was printed in the *Philosophical Transactions*. Jenner's story was accepted by naturalists, including Charles Darwin, but to Creighton the whole thing seemed merely absurd. To begin with, various quite respectable ornithologists, who had actually written books on the subject, said nothing about it. Then it was very suspicious that Jenner should make this discovery suddenly. "All this varied, rich, and marvellous experience of the behaviour of young cuckoos has to be crowded into a few days at the end of the breeding season of 1787, having eluded the observer's notice during all the years since 1773, when he first wrote to Hunter about his 'observations on the cuckoo.' Hunter's advice to him on that occasion was, 'Be as particular as you possibly can,' and never was the advice more needed." So our critic concludes: "Jenner's cuckoo paper contains a few credible and prosaic facts: but the greater part of it, and all that part of it which is best remembered, is a tissue of inconsistencies and absurdities."

Now it would undoubtedly be very suspicious if a learned man who had spent ten years in collating a manuscript had sent his work to the press, then withdrew it, and re-presented it with a

score of revolutionary new readings which he had only made out in the last few weeks. Manuscripts will obligingly stay put. But birds and beasts will not. I remember Creighton pointing out to me more than a quarter of a century ago that Gilbert White himself had quite erroneous ideas about the size of the cuckoo's eggs. "You wonder, with good reason," wrote Gilbert White, "that the hedge sparrows, etc., can be induced to sit at all on the egg of the cuckoo without being scandalized at the *vast disproportioned size* of the supposititious egg; but the brute creation, I suppose, have very little idea of size, colour, or number" (fifth letter to Barrington). The italics are mine. There used to be an exhibit in the Natural History Museum which illustrated the fact that there is *not* a vast disproportion between the sizes of the eggs, and it was an early piece of biometry in this country to show that there was a correlation between the size of the egg of the cuckoo and that of the egg of the foster-parent.\* It would seem that even Gilbert White did not have very frequent opportunities of comparison; one must depend a little on luck in natural-historical studies.

That consideration probably occurred to the ornithologists who accepted without demur the "tissue of inconsistencies and absurdities." However, when Creighton wrote, it could not be proved that the ornithologists were right in accepting Jenner's statements. I suppose it cannot be *proved* even now that Jenner did not invent the whole story. But, since a moving picture has been taken of a young cuckoo ejecting its foster-brother from the nest, and photographs of young cuckoos conforming to Jenner's description of their structure have been exhibited at a meeting of a learned society, we should have to credit Jenner with an imaginative prescience which even Baron and Simon might have hesitated to postulate. It rather looks as if the "tissue of inconsistencies and absurdities" had entangled not Jenner but his magisterial critic.

On the strength of this lucky piece of observation, Jenner was elected F.R.S. (February 1789).

"It is one of the evils of making a man a Fellow of the Royal Society," writes Creighton, "that people will be apt not to recognize any subsequent nonsense that he may write, in the name

\* See Letter, *Biometrika*, Vol. I, 1901, p. 164.

of science, for what it really is." It was, perhaps, a little naïf of Creighton to attribute so much prestige to the letters F.R.S. even in his generation or ours. After all, Alfred Russel Wallace was not only F.R.S. but one of the most famous men of science of his generation; he wrote a good deal of what Creighton no doubt considered very good sense about Jenner and his work. But very little attention was paid to it. That, in the eighteenth century, fellowship of the Royal Society would secure a man the ear of the public on all scientific questions seems improbable. But it does seem probable that the addition of the letters F.R.S. to the name of a country apothecary was of some importance, and in a few years Jenner ceased to be a country apothecary. He sold his general practice in 1792, obtained the degree of M.D. from St. Andrews, and did a little consulting practice in Cheltenham. He had inherited some money and spent his time between Berkeley and Cheltenham. From an early biographer (Fosbrooke) we learn that "it was chiefly during these periods of residence in Berkeley and Cheltenham (because he was not then burdened with the labours which vaccine had generated) that Dr. Jenner used to amuse himself with extemporaneous effusions in poetry not intended for the press. In this way his taste generally took an epigrammatic turn, but was strictly confined to harmless gentlemanly facetiousness."

It was also during this time that the "masterpiece of medical induction" was prepared.

Edward Jenner, M.D., F.R.S., aged forty-five, was a different person from the young country apothecary whose clumsy fingers John Hunter had once damned, who had been advised by John Hunter to speculate less and experiment more; also the great biologist was no longer able to give frank and friendly criticism; he died in 1793. In 1797, Jenner sent to the Royal Society a manuscript entitled "An Inquiry into the Natural History of a Disease known in Glostershire by the name of the 'Cowpox,'" which was rejected—"the perusal of his cases and experiments produced no conviction whatever, and he received a friendly admonition in reply, that as he had gained some reputation by his former papers to the Royal Society, it was not advisable to present this one, which would injure his established credit."\*

\* Crookshank's *History and Pathology of Vaccination*, Vol. I, p. 138.

Jenner revised and extended his paper, which appeared in pamphlet form in 1798. Its title, more amplified than its contents, now read: "An Inquiry into the Causes and Effects of the Variolae Vaccinae, A Disease, discovered in some of the western counties of England, particularly Gloucestershire and known by the name of the Cow Pox."

This is the "masterpiece of medical induction," the fruit of thirty years' thought, observation, and experiment. It is not necessary to be technical or dogmatic in order to make the issues clear.

It had long been held that second attacks of smallpox were rare. Cases of second or even third attacks had indeed been recorded on reliable evidence, but they were rare, and persons who had had the smallpox were able to nurse patients with impunity and to submit to inoculation with the matter of smallpox with impunity. This latter observation was made when at the beginning of the eighteenth century the plan of inoculating the smallpox was introduced into Western Europe. The idea was that, since the smallpox was almost as common as the measles now, it was better to go through with it at one's own convenience and in the most favourable circumstances, rather than wait for casual infection. There were, however, two practical objections. The first that inoculated smallpox might, and sometimes did, kill the patient; the second that the inoculated person might prove a source of infecting unprotected persons. Ways and means were found by inoculators to reduce both risks by what would now be called a method of attenuating the virus, but there was a suspicion that some of the inoculators had attenuated the virus out of existence, since some of their clients caught natural smallpox and died of it.

Jenner's starting-point was a superstition, tradition, or whatever the reader likes to call it, that persons who had caught from the cow an infection which had—again, as the reader pleases—some superficial resemblance to or a striking analogy with smallpox, were thereby rendered incapable of taking smallpox. Whether this cowpox were a loathsome disease or a trifling inconvenience it was quite certainly not dangerous to human life. If, therefore, when naturally acquired it *did* confer immunity, and if it could be inoculated from cow to man and then from man to man without inconvenience, it would follow that cow-

poxing rather than smallpoxing might advantageously replace the latter process as a preservative against the natural smallpox. These two propositions, viz. (1) that immunity is conferred by naturally acquired cowpox; (2) that cowpox can be carried on from arm to arm, and so carried on will confer immunity, are of fundamental importance. These must be made probable by induction. Jenner, indeed, surmised that the origin of both cowpox and smallpox was to be found in a third morbid process observed in horses and known as the horse-grease; but, at a very early stage in the history, this doctrine was completely discredited. Such part of the "Inquiry" as is devoted to it can be neglected; its only importance for us is that, *pro tanto*, it lowers Jenner's credit.

To found the induction that an attack of natural cowpox confers immunity against smallpox Jenner cited fourteen cases, covering about twenty persons. The interval between the natural attack and a test inoculation of smallpox matter varied from fifty-three years to nine months, and in every case the test inoculation failed. Without going into technicalities, I may say that what Jenner claimed to have done was to apply to the cowpoxed persons exactly the same process of inoculation as was ordinarily used for prophylactic purposes, and to have discovered that the local reaction was transitory, i.e. that no fluid-containing vesicle was produced on the skin, and that there was no constitutional disturbance. Assuming that Jenner's inoculation test was valid, it would seem a little optimistic to "presume it may be unnecessary to produce further testimony in support of my assertion that the cowpox protects the human constitution from the infection of the smallpox." It must have been known to Jenner that some persons had a natural immunity to smallpox, and even if we agree that such natural immunity is rare, it might have seemed prudent to inquire whether any of the twenty persons on whom he reported had ever been in contact with patients suffering from natural smallpox. This is a modest outcome of so many years' alleged inquiry. The record disposes of the mythical incessant thought and watching.

The second proposition depends upon two experiments, one involving a single, the other more than ten persons. In the first experiment a child was inoculated with matter from a sore on

the hand of a naturally cowpoxed dairymaid; this child subsequently proved insensitive to the smallpox inoculation test. The second experiment involved a series of inoculations. A child was inoculated with matter from the nipple of a cow; from this child's arm another child was inoculated; from this child several others were infected, and the process was carried to a fifth remove from the cow. To the whole of the subjects of this experiment the smallpox inoculation test was not applied; in fact, it was only tried on three, viz. the first child in series (the one infected directly from the cow), the next in series, and the last, i.e. the boy whose cowpoxing was at the fifth remove from the cow. In these three trials the results were negative.

This, again, is a modest number of experiments, but assuming good faith on the part of the experimenter, would create a presumption that arm-to-arm perpetuation of the virus was practicable and conferred a measure of immunity. I think that anybody who without other knowledge of the subject compared this paper not with famous classics such as Harvey's *Exercitatio* but with, for example, William Hewson's papers on the coagulation of the blood (Hewson was also a pupil of John Hunter) would have no difficulty in reaching the conclusion that it was not a "masterpiece of medical induction" but just the sort of rambling, discursive essay, containing acute observations mixed up with mere conjectures, which an unsystematic field naturalist might be expected to produce. It has none of Gilbert White's literary charm, but it *does* remind us of his speculations. "May it not, then, be reasonably conjectured that the source of the smallpox is morbid matter of a peculiar kind, generated by a disease in the horse, and that accidental circumstances may have again and again arisen, still working new changes upon it, until it has acquired the contagious and malignant form under which we now commonly see it making its devastations amongst us. And, from a consideration of the change which the infectious matter undergoes from producing a disease on the cow, may we not conceive that many contagious diseases now prevalent among us may owe their present appearance not to a simple but to a compound origin? For example, is it difficult to imagine that the measles, the scarlet fever, and the ulcerous sore throat with a spotted skin have all sprung from the same source, assuming some variety in their

forms according to the nature of their new combinations? The same question will apply respecting the origin of many other contagious diseases, which bear a strong analogy to each other." That is Jenner. Gilbert White, having observed a "miserable pauper who, from his birth, was afflicted with a leprosy," confides to his friend Barrington (thirty-seventh letter to Barrington) that the eradication of leprosy must be a matter of wonder and satisfaction to a humane and thinking person. Such a person will, "when engaged in such a train of thought, naturally inquire for the reason. This happy change perhaps may have originated and been continued from the much smaller quantity of salted meat and fish now eaten in these kingdoms; from the use of linen next the skin; and from the profusion of fruits, roots, legumes, and green, so common in every family. . . . One cause of this distemper might be, no doubt, the quantity of wretched fish and salt fish consumed by the commonalty at all seasons as well as in Lent; which our poor now would hardly be persuaded to touch."

In matter as well as manner the advantage is with the curate, not with the M.D., F.R.S. The doctrine that the horse not only led us to gamble but was ultimately responsible for our children getting smallpox, measles, scarlet fever, and diphtheria did not outlive Jenner; the late Sir Jonathan Hutchinson was an enthusiastic exponent of a fishy origin of leprosy.

Indeed, it seems a fair presumption that had Jenner been left to himself the masterpiece of medical induction would have had about as much effect upon the medical world as Gilbert White's meditations on leprosy. Whether it was that, as Hunter said, Jenner had damned clumsy fingers, or that his good luck deserted him, the strain of vaccine matter which he carried through five removes from the cow petered out, and his attempts to raise new strains were by no means auspicious; indeed, he discovered that cowpoxing sometimes led to very bad arms indeed. At this point two other doctors come on the scene. Later on Jenner strongly suspected one, or both, of them of a desire to play him off the stage altogether. George Pearson, like Jenner, was M.D., F.R.S., but not a country practitioner; he was a College Physician, and at the time the "Inquiry" appeared, physician to St. George's Hospital and lecturer in the medical school. "His lectures," says

Munk, "were always popular, and to the last he commanded a numerous class. As a practitioner he was judicious and safe rather than strikingly acute or original. He was a sound Latin scholar, a disinterested friend, a good-humoured and jocose companion; he abounded in anecdotes, which in his lectures, equally as in society, he told with excellent effect"; in fact, an "eminent Harley Street specialist" of the best type, moving in circles very different from that of Jenner. Pearson had heard from John Hunter in 1789 that Jenner was at work on the cowpox, and Jenner's pamphlet evidently made on his mind the impression which, in my opinion, it would be likely to make on the mind of any man, viz. that a *prima facie* case had been made out, but only a *prima facie* case. Pearson therefore set about a more systematic collection of data, particularly with reference to the proposition that those who had passed through an attack of natural cowpox were immune from either inoculated or natural smallpox. To this end he adopted the questionnaire method which, since the time of Francis Galton, has been so familiar to us, and he also supervised a small number of experiments. His findings are set out in a pamphlet, printed in 1798, certainly much better adapted to "have commanded the confidence of reflecting persons" than anything Jenner ever wrote.

In the first place, Pearson gave an orderly account of the results of his inquiries directed to physicians and others throughout England. There was a consensus of opinion, supported by the citation of various particular illustrations, that the occurrence of smallpox in persons who had had an attack of cowpox was extraordinarily rare. Pearson then gave very precise particulars of the results of inoculating smallpox on five persons, three of whom had and two had not had natural cowpox. In the three cowpoxed persons no smallpox pustules were raised; in the other two, variolous eruptions (twenty or thirty pustules in one, about a dozen in the other) were produced. Unlike Jenner, Pearson very carefully discussed other possible reasons for the failure of the inoculation in the first three cases, and went no further than to conclude that "it seems most reasonable to impute the inefficacy of the variolous poison in the above three instances to a state of inexcitability produced by the cowpox poison." He systematically examines other propositions, such as Jenner's speculation that

cowpox was ultimately derived from the grease of horses. "This assertion," he says, "stands in need of support from other observations," and the result of his inquiries is shown to be very unfavourable to such a doctrine. Pearson's conclusion is that the cowpox inoculation is a sound method, *but* "I shall be no better contented with those who consider the facts to be already demonstrated than with the opposite extreme opinion, that the whole of the prospects displayed are merely *Utopian*. The fortunes of the new proposed practice cannot, with certainty, be told at present by the most discerning minds, more instances are required to establish practical and pathological truths. Without assuming pretensions which I think unwarrantable, the number of instances further requisite cannot be stated; but one may safely assert that well-directed observation in a thousand cases of inoculated cowpox would not fail to produce such a valuable body of evidence as will enable us to apply our knowledge with much usefulness in practice, and establish, or at least bring us nearer the establishment of, some truths."

Within a few months what at least seemed a fulfilment of this admirably expressed desire was provided by Dr. William Woodville. Woodville, like Pearson, was a College Physician, but less eminent in his profession. He at one time practised in his native county of Cumberland, but came to London in 1784, and at the time of these events had been for eight years physician to the smallpox and inoculation hospitals. He was a specialist in smallpox, and a skilful inoculator. He, like Pearson, had been struck by Jenner's publication, and desired to try out the new method. Heaven provided him with an opportunity in the shape of an outbreak of cowpox in a dairy in Gray's Inn Lane. To the dairy he repaired in company with a veterinary student from Jenner's own parish—but Creighton tells the story so well that I cannot do better than quote him: "In a day or two the milkmaids had the blebs on their fingers, exactly as Jenner had figured in his first plate. The original sceptics and rejecters of Jenner's innovation, Sir Joseph Banks, Lord Somerville, and others, were fetched to the cowhouse, and Jenner's book was produced. Scepticism gave way to belief, for there, sure enough, was the identical large bluish-white vesicle on a milkmaid's hand which Jenner had pictured—indeed, 'a more beautiful specimen of

the disease than that which you have represented in the first plate.' Having satisfied themselves that there was such a malady as cowpox, and that Jenner's picture of it in milkers was true to nature, they concluded that there was a *prima facie* case for giving it an independent trial. No body of Englishmen would have acted otherwise; whatever the irrationality or dialectical absurdity of the project, they would put it to an experimental test [Creighton was a Scotsman]." Woodville undertook the experiment, and although he did not cowpox the thousand desiderated by Pearson, he did operate on six hundred and published a report on some four hundred and fifty, in 1799. Woodville had no difficulty in keeping a strain of cowpox virus going; indeed, he kept several going, and his stock was probably the ancestor of all the strains now used in England. His results, however, were in one way unlike Jenner's, so different that, according to the faithful Baron, they were wellnigh fatal to the cause of vaccination. A few of Woodville's subjects were very ill, one died, and a great many had hundreds, one or two a thousand, pustules on their bodies. That was not at all what Jenner had led the world to expect; indeed, it did not come within Jenner's experience. Jenner did his experiments in a country village; Woodville his hundreds in an inoculation hospital, and inoculated many of his subjects with smallpox matter soon after he had cowpoxed them. Here is one of his series. He inoculated matter from a poxed cow upon the arm of a girl of seventeen, Jane Collingridge, and on the fifth day he inoculated smallpox matter into her other arm. Between one and two hundred pustules came out on this girl. From the cowpox vesicle on her arm another girl, Sarah Butcher, aged thirteen, was inoculated. She was smallpoxed on the sixteenth day and escaped pustules, which was the fate of Frances Jewel, a girl of twenty, cowpoxed from Butcher and smallpoxed on the thirteenth day. From Frances Jewel, Charlotte Fisk, a baby of four months, being suckled by a woman with the natural smallpox in full eruption, was cowpoxed and had about forty pustules; another baby, cowpoxed from the last and smallpoxed at some date later than the fourteenth day from the cowpoxing, had twenty pustules. Sarah Hat, aged twenty, cowpoxed from this baby, had a crop of forty pustules; when she was smallpoxed does not appear. J. Wall, aged ten years, cowpoxed from Hat and Galloway

(age not stated) cowpoxed from Wall, had no eruptions. Woodville evidently kept the ball rolling with better success than Jenner. All his patients (except an infant which died) were smallpoxed again without any further results. He expresses his conclusions in the following terms: "Were I enabled to state a number of cases of variolous inoculation, equal to those given above, and reduced to a similar tabular form, the comparative magnitude of the two diseases might be estimated with tolerable precision. It is evident, however, that the matter of the vaccine disease has generally produced much fewer pustules, and less indisposition, than that of the smallpox; for it appears from the preceding statement that about two-fifths of all the persons inoculated for the *Variolae vaccinae* had no pustules, and that in not more than a fourth part of them was there experienced any perceptible disorder of the constitution. But it must be acknowledged that, in several instances, the cowpox has proved a very severe disease. In three or four cases out of five hundred, the patient has been in considerable danger, and one child, as I have already observed, actually died under the effects of the disease. Now, if it be admitted that, at an average, one of five hundred will die of the inoculated cowpox, I confess I should not be disposed to introduce this disease into the Inoculation Hospital, because out of the last five thousand cases of variolous inoculation the number of deaths has not exceeded the proportion of one in six hundred. But I am inclined to think that if the matter of the cowpox, used for the purpose of inoculation, were only taken from those in whom the disease appeared in a very mild form, the result would be more favourable than in the statement here given."

It will be noticed that Woodville has tacitly assumed that his inoculees owed their subsequent immunity to the cowpoxing they had undergone. It did not apparently occur to him when the report was made that, apart from a risk of contamination of the lancets (which he *did* consider and exclude), the subjects might have been simultaneously cowpoxed and smallpoxed; they were dealt with in an inoculation (for smallpox) hospital, and were exposed to the natural infection of smallpox, and some were inoculated with smallpox within a few days of the cowpoxing. In a later publication he does refer to the possibility in these terms: "It is true that many of these vaccine cases were

conjoined with the smallpox from the influence probably of the variolous infection, but as the eruptive cases exhibited the genuine cowpock on the part inoculated, and the matter of it very generally propagated the vaccinia without eruptions, in private practice and in the country, it is fair to admit them into the class of cowpock cases." Actually Jenner himself used Woodville's strain, and in his practice did not reproduce the pustular eruptions. Woodville's argument might be expanded in this way. As many as two-thirds of his cowpoxed subjects had no stigmata except those of the cowpoxing, and these were as insensitive as the others to the subsequent smallpoxing; therefore we may attribute their protection to the cowpoxing and infer that the widespread eruptions on the others were an accident of cowpoxing. An enthymeme rather than a syllogism, but likely to appeal to practical men or, at any rate, to Englishmen. Creighton, indeed, thought Woodville a bit of a fool, but acquitted him of roguery. "He died," says the dialectical Scotsman, "on March 26, 1805, and as he was an honest man we may say of him that he was taken away from the evil to come."

Pearson and Woodville had, indeed, made cowpoxing practical politics, and we shall return to Jenner, whose experiences immediately after the publication of his "Inquiry" had been trying. In the first place, Dr. John Ingenhousz, an elderly Belgian, a physician of distinction, Hofarzt in Vienna, and an authority on smallpox, was staying at the Marquis of Lansdowne's country house when the "Inquiry" appeared. Ingenhousz made some inquiries in Wiltshire, and informed Jenner (1) that he doubted the proposition that cowpox protected against smallpox, (2) that Jenner was, in his view, mistaken in supposing that smallpox virus ever produced anything but just smallpox.

In the next place, Jenner and a practitioner in Stroud, Thornton, obtained matter from a new source of cowpox in the village of Stonehouse. Jenner's vaccinations produced bad arms, Thornton's both bad arms and no insusceptibility to smallpox inoculation. Instead of satisfactory vesicles one had "sordid and painful" ulcers.

The importance of the Ingenhousz incident was that professionally Ingenhousz carried very heavy guns. It is not certain that Ingenhousz thought that Jenner's cowpox doctrine *was* all

nonsense. Jenner sent a friend of his, Paytherus, to interview the great man, and in Paytherus' letter to Jenner (December 14, 1798) the following passage occurs: "Dr. Garthshore has also at Dr. Ingenhousz's request written to Dr. Pulteney, of Blandford, who in reply has assured him that the inoculators of his neighbourhood have known many instances of the smallpox happening after the cowpox. He believes that it does in many instances produce that change in the human constitution as to render it unsusceptible of the smallpox but not with certainty in *all* cases. He would not hear a word in defence of your opinion respecting its origin."

The last "he" in this passage certainly refers to Ingenhousz; the last "he" but one may refer either to Pulteney (who, we know from Pearson's brochure, held that opinion) or to Ingenhousz himself. Had Jenner been the really cautious reasoner of the Baron-Simon saga, or the subtle rogue of the Creighton saga, he would have seized the opportunity of withdrawing from what either a cautious reasoner *or* a rogue should have realized to be a certainly dangerous and possibly untenable position. He would have claimed no more than that cowpoxing was as efficient as and less dangerous than smallpoxing. Actually he replied to a man twenty years his senior and of European reputation just as Miss Pross replied to Mr. Lorry. "'I don't want dozens of people who are not at all worthy of Ladybird, to come here looking after her,' said Miss Pross. '*Do* dozens come for that purpose?' 'Hundreds,' said Miss Pross." Even so Jenner to Ingenhousz: "At present, I have not the most distant doubt that any person who has once felt the influence of perfect cowpox matter would ever be susceptible of that of the smallpox."

Creighton said that Ingenhousz, who declined to enter on a further discussion, could naturally only look on such a man as either a fool or a knave. The former, perhaps, or it may be that the experienced man of the world would think him an ignorant enthusiast, in spite of the F.R.S. and M.D. Ingenhousz died the following year. What he thought of Pearson and Woodville—he lived just long enough to read them—is undisclosed.

The Ingenhousz business was troublesome, but the Stroud affair might have been fatal. Jenner had committed himself to the dogma that cowpox was an absolute preventive of smallpox:

it took him more than ten years' experience and an attack of smallpox in an aristocratic patient whom he had himself vaccinated to reach the, one would have supposed, obvious position that judgment must be based not on absolute dichotomies but on a balance of probabilities. Therefore he had to believe that cowpox which did not protect against smallpox was "spurious" cowpox, and the Stonehouse series must have convinced him that the differentiation of the "spurious" variety was going to be a chancey business, and that inoculated cowpox, whether "true" or "spurious," might lead to very bad arms. Woodville's experiment and Jenner's own experience with Woodville's lymph cleared away the last difficulty. And now we come to a very painful theme. "At an early stage in the history of his observations," wrote Crookshank, who had as low an opinion of Jenner as Creighton, but less literary ability to express it, "Jenner had hopes of his discovery proving a financial success." Crookshank quotes the following damning evidence from Jenner's diary: "While the vaccine discovery was progressive, the joy I felt at the prospect before me of being the instrument destined to take away from the world one of its greatest calamities, blended with the fond hope of enjoying independence and domestic peace and happiness, was often so excessive that in pursuing my favourite subject among the meadows I have sometimes found myself in a reverie."

It would, of course, be painful to any leading citizen of the twentieth century to entertain the thought that a doctor, actually a Fellow of the Royal Society, should have fallen so low as to dream of making money out of a public service; but, after all, Jenner belongs to the eighteenth century. Jenner's nephew, George, warned his uncle early in 1799, that is after Pearson's pamphlet was out, that if he did not bestir himself, Dr. Pearson would become the "chief person known in the business, and consequently deprive you of that merit, or at least a great share of it, which is so justly your due." Jenner—it sounds horrible in these times—promptly suggested to a friend that the Press might be worked that "some neatly drawn paragraphs" might "appear from time to time in the public prints, by no means reflecting on the conduct of P., but just to keep the idea publicly alive that P. was not the author of the discovery—I mean cowpox inocula-

tion." As Pearson had said early in his pamphlet: "I entertain not the most distant expectation of participating the smallest share of honour on the discovery of facts. The honour on this account, by the justest title, belongs exclusively to Dr. Jenner." Jenner may seem a little over-anxious. Still it is a fact that Pearson set about organizing an institution for inoculation of cowpox with himself in the chief place, and he, perhaps, was not quite so tactful as a London physician should be in offering to make Jenner an "extra corresponding physician" of it. Jenner's refusal of this dazzling honour was conveyed in what Crookshank termed a "hasty letter"; more worldly wise men might have written quite as hastily. Jenner succeeded in scotching the plan, and drew up a scheme of his own. He never forgave Pearson, who gradually cooled and finally (according to Jenner) became actively hostile to cowpoxing. For a while things went well with Jenner; in 1802 Parliament voted him £10,000, and in 1803 the Royal Jennerian Institution was founded with himself as President. Jenner then settled in London. But neither as director of an institution nor as a West End physician was Jenner a success. He quarrelled with the executive officer of the Royal Jennerian Institution (which, within five years, had, according to Crookshank, practically collapsed), and the outcome of his London consulting practice was an annual loss of £1,000. His professional colleagues were very ready to speak of Jenner in the highest terms, but less ready to admit him to their innermost circle. The University of Oxford took some coaxing (according to Creighton) to make him a Doctor, and the College of Physicians never admitted him at all. When, in 1807, after Jenner had received a second public grant—this time of £20,000—it was decided to establish a national vaccine institution, Sir Lucas Pepys—faithfully enough portrayed by Dickens as the Parker Peps of *Dombey and Son*, an eminent Harley Street specialist of the worst kind, did say to Jenner in his best manner, "You, sir, are to be the whole and sole director. We (meaning the board) are to be considered as nothing: what do *we* know of vaccination?"

It was undoubtedly true that Sir Lucas knew nothing whatever of vaccination, and equally true that he and the rest of the board did very little except draw honoraria—the Vaccine Board was one of the jobs subjected to parliamentary investigation in 1827—

but one of the things they did do was to prevent Jenner having any power at all, so that he resigned within a year. Most of Jenner's time during the last twenty years of his life was spent in attempting the impossible, i.e. in attempting to convince his correspondents that no properly cowpoxed person *could* get smallpox. What a dance it led him! For some time he clung to the "spurious" cowpox straw, but when everybody knew that most, perhaps all, vaccinations were done with the descendants of the Woodville strains which Jenner had himself blessed, this straw was useless. If, then, the vaccine were genuine cowpox and still did not always prevent smallpox, how could Miss Pross still believe her dogma? Clearly, by supposing that the vaccinator had blundered. She did suppose it. "A great number, perhaps the majority, of those who inoculate are not sufficiently acquainted with the nature of the disease to enable them to discriminate with due accuracy between the perfect and the imperfect pustule. This is a lesson not very difficult to learn, but unless it is learnt, to inoculate the cowpox is folly and presumption." That was in 1804; from being "not very difficult to learn," vaccination soon became "a science far more difficult to understand than variolation," and we hear of "that wise discriminating power without which no man can be a perfect vaccinist." But it was all in vain; perhaps the gods really did love Jenner, for they chastened him. On May 26, 1811, the Hon. Robert Grosvenor, whom Jenner himself had vaccinated ten years before, fell ill with the smallpox; the eruption "increased prodigiously, and some of the worst symptoms of a malignant and confluent smallpox showed themselves." The boy recovered, but "the noise and confusion this case has created is not to be described. . . . The town is a fool—an idiot, and will continue in this red-hot-hissing-hot state about this affair till something else starts up to draw aside its attention. I am determined to lock up my brains, and think no more *pro bono publico*; and I advise you, my friend, to do the same: for we are sure to get nothing but abuse for it." The spirit of Miss Pross is, for a moment, exorcised, and Jenner writes like a man of science: "Take a comprehensive view of vaccination, and then ask yourself what is the case? You will find it a speck, a mere microscopic speck on the page which contains the history of the vaccine discovery. In the very first thing I wrote upon the subject, and many times

since, I have said the occurrence of such an event should excite no surprise; because the cowpox must possess preternatural powers if it would give uniform security to the constitution, when it is well-known the smallpox cannot; for we have more than one thousand cases to prove the contrary, and fortunately seventeen of them in the families of the nobility. We cannot alter the laws of nature; they are immutable."

Pearson or Woodville might have written like that, but it would have been a *little* difficult for Jenner to have pointed out which passages in "the very first thing" he wrote *did* convey the warning. "*At present I have not the most distant doubt that any person who has once felt the influence of perfect cowpox matter would ever be susceptible of that of the smallpox.*"

Perhaps the thought that Pearson and not he had the right to talk so stimulated him to hound on James Moore of the National Vaccine Establishment to attack Pearson: "It is a very important part, and justice demands the exercise of severity. It must begin with the Petworth business. This is given by Lord Egremont. Next his uniting with Woodville, and forming (without mentioning the latter to me) his institution. His cajoling the Duke of York to be patron. The Duke's disgracing him. His spreading the smallpox through the land and calling it the cowpox, explaining *mechanically* the reason why it had changed its character." There is not much of the ingenuous naturalist left; ten years' celebrity had done its work. The rest of the story is little more than a repetition. Miss Pross was quickly herself, and nothing shook her faith again. On the back of an envelope dated January 14, 1823, Jenner wrote: "My opinion of vaccination is precisely as it was when I first promulgated the discovery. It is not in the least strengthened by any event that has happened, for it could gain no strength; it is not in the least weakened, for if the failures you speak of had not happened, the truth of my assertions respecting those coincidences which occasioned them would not have been made out." Faith could go no further; twelve days later Edward Jenner died.

No man has ever lived a life more open to the unfavourable criticism of a dour intellectual, but fifty-six years were to pass before that work of hostile criticism was to be efficiently done. In the meantime the immortal gods had allowed to be prepared

a few pitfalls for the critic, reserving one until he too should have committed himself too deeply for retraction. There was nothing of the ingenuous naturalist about Charles Creighton. I only knew him in later life, when he was already turned sixty, and one of the most learned men in England. His great classic the *History of Epidemics in Britain* had been published more than ten years. He himself was frowned upon by most of his professional contemporaries. He was "Creighton, *the anti-vaccinator*"—and what more was there to be said? If his spirit *was* wounded by the ostracism of persons most of whom had learned all they knew of the history of epidemic diseases either from the book he wrote or the book he translated (Hirsch's immense work), he never showed the wound. There cannot have been many better literary anecdotists than Creighton; he seemed to have read everything and expounded theories of authorship and explanations of mysteries in theological literature with as much zest and confidence as epidemiological doctrines. He knew who wrote Revelations, who *The Beast* was (I think it was S.P.Q.R.), and was quite sure that the *four* beasts were the prophets Isaiah, Jeremiah, Daniel, and Ezekiel. It would have taken a *very* well-read man to stand a chance with him in a literary tussle, but he did not bully young people. He had a sense of fun, but his table-talk suggested a certain aloofness from, even a contempt for, current medical thought. That was, perhaps, natural enough in a man whom his contemporaries had treated so ill; but it did not seem quite so easy to explain as all that. I heard a friend, more nearly of his generation than I was, say, "Creighton always prefers the possible to the probable," and it was a profound remark. His *magnum opus* had been finished (in 1894) when bacteriology was still a young, scientific method, but had already led us to important truths. The only direct notice of the "microbic theory" he took, however, was to insert a footnote to his chapter on Asiatic Cholera, after a funny story about a millhand, the following words: "The common microscopic objects uniformly found in choleraic discharges by later observers have been vibrios, of which half a dozen, or perhaps a dozen, varieties have been distinguished. One of these was somewhat audaciously named the 'cholera germ' or 'comma bacillus of cholera,' by Dr. R. Koch, who went to Calcutta in 1884. All vibrios which have a corkscrew form when in motion, are apt

to assume the comma form when at rest.”\* So that was that! It was a few years after Creighton’s book was published that Kitasato—somewhat audaciously—named the bacillus of plague; but in 1891 the germ theory was in the air—in more senses than one—and Creighton smote it good and hard.

“It is our duty to construct the best hypothesis we can, sparing no labour. No one really dispenses with theory, whatever his protestations to the contrary; those who are loudest professors of suspended judgment are the most likely to fall victims to some empty verbalism which hangs loose at both ends, some ill-considered piece of argument which ignores the historical antecedents and stops short of the concrete conclusions. It has been so in the case of infective diseases, and of bubo-plague in particular. The virus of the plague, we are told, is specific; it has existed from an unknown antiquity, and has come down in an unbroken succession: we can no more discover how it arose than we can tell how the first man arose, or the first mollusc, or the first moss or lichen; its species is, indeed, of the nature of the lowest vegetable organisms. The objection to that hypothesis of plague is that it involves a total disregard of facts. It is a mere formula, which saves all trouble, dispenses with all historical inquiry, and appears to be adapted equally to popular apprehension and to academic ease.”†

Indeed, the truth had been reached long before this fact-disregarding formula had been promulgated. The plague virus was generated by the corruption of the dead; that was suspected already in the sixteenth century, but “the most brilliant exposition of it, one of the finest exercises of diction and of reasoning that has ever issued from the profession of medicine, was that given for the origin in Egypt of the great plague of Justinian’s reign by Etienne Pariset, Secretary to the Académie de Médecine and commissioner from France to study the plague in Syria and Egypt in 1829.”‡ In the same admirably clear style, Creighton resumes Pariset’s argument and tests it by modern instances: always he finds a correlation in both time and place between the occurrence of plague epidemics and of cadaveric decomposition in the soil. He called attention to the fact of rats leaving

\* *History of Epidemics in Britain*, Vol. II, p. 827.

† *Ibid.*, Vol. I, p. 174.

‡ *Ibid.*, p. 156.

their holes when the plague broke out "so abundantly confirmed from the recent plague spots of Southern China, of Yun-nan, of Jumaon, and of Gujerat."\* He quotes Thomas Lodge writing in 1603 to the same effect.† "That," he writes, "is only one of many proofs that the virus of plague has its habitat in the soil, although it may be carried long distances clinging to other things. In its most diffusive potency it is a soil poison generated, we may now say with some confidence, out of the products of cadaveric decay."

It is easy enough to be wise after the event. Perhaps an ideal deductive reasoner might have lingered over the rat business, might have considered the alternative that it was not the rat driven to the surface by the soil poison but the rat carrying within him the poison which started the train of events. Perhaps Socrates might have wanted a little more precision in the description of this soil poison. But I do not think there are many people—I am sure I am not one of the exceptions—who, if they had read Creighton's description in 1891, would have failed to be impressed by its cogency. The same readers coming to the passage for the first time in 1931 would be apt to wonder how *anybody* could reach such totally erroneous conclusions. Such a judgment would, of course, be a pure anachronism, yet would have this kernel of truth, that the pure reasoner may rashly assume that *his* facts, because they are more numerous than those of empiricists whom he despises, are the only facts which matter. Certainly Creighton did, like the Hellenistic Greeks, overrate deductive reasoning and had all Galen's contempt for mere empiricists. Further, he could not really believe that other men were different from himself, and so he came to believe that behind the happy-go-lucky empiricist lurked the unscrupulous rogue.

Early in his exposure of Jenner he regrets that the medical profession of 1798 did not know the real history of the business, for then "they would probably have found out Jenner to be the *vain, imaginative, loose-thinking person that he certainly was by nature*, and they might have so acted as to prevent him from becoming the impostor and shuffler that the course of events made him." The words I have italicized seem to me an accurate

\* *History of Epidemics in Britain*, Vol. I, p. 172.

† Creighton does not call attention to the fact that Lodge was merely copying from Avicenna.

psychological diagnosis, and substituting for "impostor and shuffler," "fact-blind enthusiast," the rest might stand. But Creighton's Jenner ceased to be a vain, imaginative, loose-thinking person, and became an impostor and shuffler before the "master-piece" was published. Why, he secured his Fellowship of the Royal Society by fabricating incredible observations of the cuckoo! It is, however, with regard to the title-page of the "Inquiry" that Creighton really expands. On that title-page, Jenner gave *Variolae vaccinae* as the name of cowpox. If we hold fast to the "vain, imaginative, loose-thinking" hypothesis, there is not much difficulty in understanding what happened. Compulsory Latin has gone, but even now a faint flavour of respectability lingers about a Latin quotation, while entomologists and other naturalists still prefer (for excellent reasons) Latin to vernacular nomenclature. In the eighteenth century Latin was *extremely* respectable, and it would not argue much vanity to suppose that a doctor would like something a little more respectable than cowpox for the name of his subject, just as he liked a not particularly appropriate quotation from Lucretius\* on the title-page. It is not a very wild speculation to believe that Jenner's neighbour, the Rev. T. D. Fosbroke, supplied both (the reverend gentleman defended the classical propriety of the title in print and with some asperity).

Creighton will not hear of this simple explanation. His theory is that Jenner invented the phrase *Variolae vaccinae* in order to insinuate into the minds of his medical readers that cowpox was smallpox, and that he actually succeeded in this scheme. There are at least thirteen denunciations of this roguery in Creighton's book. On page 44 it is a "startling novelty." On page 52 "the name of *Variolae Vaccinae* on the title-page" has become "Jenner's master-stroke." On page 73 Creighton has reached the conclusion that "the name of *Variolae Vaccinae* was accepted as proof enough that cowpox *was* a sort of smallpox of the cow." On page 76 we read of the "unblushing invention of the misleading name of *Variolae Vaccinae*." By page 79 Creighton has become, for a moment only, doubtful whether he may not have made too much of this and, with the candour which never deserted

\* "What surer test can we have than the senses, whereby to note truth and falsehood?" Jenner was not a *very* thoroughgoing exponent of the experimental method.

Creighton, points out that Pearson specifically objected to the title as being inexact (this it was that provoked the Rev. T. D. Fosbroke's letter) and writes: "It must seem strange to anyone who reads Pearson's "Inquiry" now that it should not have sufficed at the time to show up the artifice of Jenner in renaming cowpox 'variola vaccinae' or smallpox of the cow." The reason this did not happen was that Pearson, having come to the conclusion that cowpox might be used as a prophylaxis, did not think it worth while to continue the verbal discussion. It was not Pearson's evidence in favour of cowpoxing, but Pearson's ceasing to object to the new name for cowpox, which did the mischief!

On page 118 the name has become an "unwarrantable liberty," and (page 122) Woodville only went on with his work because the *name* misled him. And so on, and so on, until on page 241 we read: "It was Jenner, and Jenner alone, who called the cowpox, 'smallpox of the cow,' having insidiously placed the name in Latin on the forefront of his "Inquiry," and then carefully abstained in the preface and text from ever once saying that he had given the disease of the cows and milkers a new name, or why he had given it a new name. Even so trenchant a critic as Verdier was hardly prepared to find that an Englishman, whose designation of F.R.S. proclaimed him to be of academical rank, should be wanting in the rudiments of common candour. The trick of the title-page had relatively more effect in France than elsewhere; it implanted an illusory idea as to the nature of cowpox, which at once found expression in the French name, and became the more fixed in the minds of the French profession of medicine by reason of their having none of those first-hand experiences of the shocking nature of cowpox in the cow which the English were not wanting in."

There was not much resemblance between Jenner and Creighton, but that Creighton should believe all this, should really believe that the two words *Variolae vaccinae* had this power, argues a capacity for belief not short of Jenner's own. The invention of the name was, perhaps, the most damning proof of Jenner's roguery, but his recommendation of the variolous test was almost as criminal. Putting this rather technical matter as shortly as possible, Creighton's indictment was this: that the method of

inoculating smallpox matter enjoined by Jenner was such that, whether the patient had or had not been cowpoxed, no result worth talking about was likely to follow. If that were so, if the test were really a bogus one, it seems a little hard to jeer at Jenner for having often enough omitted to try it and to comment on one of Jenner's favourite cases in the following terms: "Poor Phipps, as Jenner used to call him, was inoculated some twenty times after that, and never 'took'; he was Jenner's show case of resistance to smallpox; he was a poor consumptive or scrofulous youth with his lymphatic glands so clogged [after the cowpox?] that any subsequent inoculation of virus on the arm had no chance of being absorbed."

The implicit doctrine that consumption confers an immunity against smallpox virus is a little startling, but if the inoculation test was a bogus one then there was no virus to absorb, and why explain what *ex hypothesi* needs no explanation? Assuming that Jenner *did* deliberately select a bogus test, it seems *a priori* odd that others should have followed him without question. Pearson and Woodville, even Creighton *teste*, were honest men, and both, more particularly Woodville, thoroughly familiar with the signs and symptoms of inoculated smallpox, yet they both came to the conclusion that the variolous test *after* cowpoxing gave a different result from the test applied before cowpoxing. Creighton is puzzled. "The profession were undoubtedly mystified and hoodwinked about the true nature of cowpox; they were started off on an entirely false analogy by Jenner's adroit title-page. But I can find no excuse for their conduct over the testing inoculation with smallpox on the result of which it was generally agreed that the verdict would turn. If any of my readers or critics having taken the trouble to go over the evidence at first hand will make out a case more favourable to the leaders and editors of medical opinion at this juncture, I shall be ready to amend the result of my own investigation, finding it somewhat incredible as it stands." Could the explanation possibly be that Pearson, Woodville, and the other "leaders" when they asserted that the reaction of the cowpoxed person to the test—whether "bogus" or not—differed appreciably from the reaction of a person who had not been vaccinated, were actually telling the truth? That this might be the explanation is rather suggested by the discovery made after

Creighton's book was written, that Jenner's "entirely false analogy" between cowpox and smallpox was quite exact.

The hardest thing to swallow in connection with the cowpox business was a belief that a person *could* be protected from one disease by giving him "another" disease. "The cowpox poison," wrote Pearson, "appears to alter the human constitution so as to render it unsusceptible of the agency of a different morbidic poison, namely of the variolous, in producing the smallpox. This fact is, I believe, quite a novelty in physiology and pathology; it indicates a new principle in the mode of prophylactic practice." He left it at that. This was the pure empiricism so repugnant to the mind of Creighton, and the basis of cowpoxing remained purely empirical until nearly eighty years after Jenner's death; nobody had unequivocally succeeded in turning smallpox virus into cowpox virus or establishing anything but a purely empirical and indirect connection between them. Creighton's predecessors, with less skill but even greater vehemence than he, rubbed this "absurdity," this "entirely false analogy," in. Creighton did *his* best to demonstrate that the "true" analogy was not between cowpox and smallpox but between cowpox and the unqualified pox, viz. syphilis. Then, in 1902, Dr. S. Monckton Copeman inoculated a monkey with smallpox virus, vaccinated a calf from the monkey, and produced—typical cowpox. Twenty-three years later Dr. Mervyn Gordon published a long series of experiments which will be still more attractive in these days of scientific detective fiction. We have all heard how the Dr. John Thorn-dykes can decide whether it was really A's blood on the knife, as B said it was, by injecting some of A's blood into an animal and then mixing some of that animal's blood with washings from the knife.

An analogous process will track down viruses. Our experimenters took into consideration three viruses, that of vaccinia (now we have reached our own age, we may substitute the polite vaccinia for the vulgar cowpox), that of smallpox, and that of chickenpox, and this is what they found; if an animal had been injected with vaccinia its blood would react with either smallpox virus or vaccinia virus, but not with chickenpox virus. Vaccinia *is* tested to protect monkeys *better* against two strains of variola *than* either strain against the other. So Creighton's neat sarcasm that "the single

bond connecting cowpox with smallpox was the occurrence of the word 'pox' in each name" proved at long last to be itself—"some empty verbalism which hangs loose at both ends," the "entirely false analogy" was an exactly correct analogy; the vain imaginative, loose-thinking person had, blunderingly and rashly, reached a true conclusion. *Variolae vaccinae* was the right name, after all.\* It showed a sense of humour in the immortal gods to hold up that discovery so long; cynical humour, perhaps, because many people have reasoned as loosely as Jenner and *not* guessed any truth worth the having and, in this age, the habits of mind and the intellectual outfit of a Creighton, not of a Jenner, are to seek. To the question whether vaccination is a practically valuable prophylaxis, the formal proof of the kinship of vaccinia and variola is very nearly irrelevant; the question has been settled by reasoning with which Creighton had no sympathy and Jenner would not have understood. But that is not part of Jenner's story.

#### RECOMMENDATIONS FOR FURTHER STUDY

All the quotations from Jenner's writings and those of his contemporaries are taken from Crookshank's *History and Pathology of Vaccination*, London, 1889, the second volume of which consists of reprints of the original documents. All the quotations from Creighton (except those distinguished in the footnotes) are from *Jenner and Vaccination*, London, 1889.

- \* See Reports Nos. 98 and 143 of the Medical Research Council.

## IX

### THE POST-JENNERIAN CONTROVERSY

In the previous chapter I have tried to make plain the human elements of the vaccination controversy. Most of the amateur pro-vaccine enthusiasts (whether medically qualified or not) base their faith on the conception of Jenner as a transcendent scientific genius; most of the anti-vaccinist enthusiasts take as a fundamental datum the conception of Jenner as a super-crook. I have tried to convince the reader that neither faith is true.

When we return from the emotional to the logical consideration of our subject and seek to learn whether cowpoxing as a matter of empirical fact did and does diminish, (a) the individual's risk of taking smallpox if exposed or of dying of smallpox if attacked, (b) the crowd's risk of having much or fatal smallpox when a large proportion of its members has been cowpoxed, it is found not to be easy to keep clear of emotional mystifications. In my opinion, evidence relating to proposition (a) is less ambiguous than that relating to (b).

In this matter of smallpox prophylaxis by vaccination no straight control experiment has ever been done, but indirect evidence of a statistical kind, that vaccinated persons when exposed to the same risk of taking smallpox as vaccinated persons were attacked at a lower rate, and that those who *were* attacked died at a lower rate, began to be tendered early in the history of the subject, and, so far as I know, all large published collections of data have brought out a decided advantage on the side of the vaccinated. It is clear that evidence respecting *fatality* is likely to be simpler than evidence respecting *incidence*, because it is always open to an objector to say that the opportunities of the vaccinated and the unvaccinated to contract smallpox were not the same. If, for instance, there were a social distinction between the vaccinated and the unvaccinated this would be much more likely to be correlated with a difference of exposure to risk of taking the disease than with a difference of resistance to the disease when acquired. For instance, typhus and bubonic plague have, for fairly obvious reasons, been, as epidemics in civil life, *morbi pauperum*, and any

social bias in the distribution of prophylactics would be serious. But in respect of fatality the bias is much smaller; indeed, in the case of typhus, some good observers hold it to be reversed, that the fatality suffered by medical and nursing attendants has been greater than that suffered by the poverty-stricken, famished peasants.

In smallpox the advantage in respect of fatality enjoyed by the vaccinated has been conspicuous, and those who have been unwilling to accept the statistics at their face-value have either had to resort to charges of dishonesty against the compilers of the data, or to arguments the ingenuity of which is more conspicuous than their cogency. An illustration of the latter class is Creighton's treatment of Gregory's observation that in the epidemic of 1825 the fatality-rate on the vaccinated attacked was only 8 per cent, upon the unvaccinated attacked 41 per cent. Creighton remarks that "there are various ways of apportioning a general average. The presence or absence of cowpox scars is one principle which could not have been used to break up the 25 per cent of 1777, or the 39 per cent of 1781, or the 33 per cent of 1796 into two component parts." He then notes that one thing common to all times is different fatalities at different ages, and remarks that "all the deaths in the 8 per cent division of 1825 were between the ages of eighteen and twenty-seven: the ages of the 41 per cent division are written in the books of the hospital." Finally, he observes that "however manifold the cutting up of a general average, some divisions would be identical, corresponding to natural lines of cleavage" (Creighton, *History*, Vol. II, p. 595). Were I as suspicious of Creighton as Creighton was of Jenner, I should suspect the last-quoted sentence to have been intended to meet the case of data wherein within the *same* age group, the vaccinated had a lower rate of fatality than the unvaccinated. Whether Gregory's statistics were or were not vitiated by a high correlation of vaccinal state and age, that criticism does not apply to such results as in Table 42, page 276.

Evidently these contrasts cannot be explained away as functions of age differences, so the rational critics had to resort to another explanation, viz. that the responsible factor is not age but social differentiation. We are invited now to suppose that, in the main, vaccinated persons belong to a better-housed and better-fed

stratum of the community, and therefore are more resistant to any acute disease.

Relevant statistical evidence on this matter is scanty, but the late Dr. W. R. Macdonell provided some. His data were supplied

TABLE 42

## FATALITY-RATES AT AGES

The upper part of the Table is based on Gayton's experience (1870-84, vide *First Report, Roy. Com. on Vacc.*, Appendix III). The lower part relates to the M.A.B. experience in 1901-2. "Doubtful" cases have been regarded as "vaccinated."

Age Group	Vaccinated			Unvaccinated		
	Number of Cases	Number of Deaths	Fatality-rate per 100	Number of Cases	Number of Deaths	Fatality-rate per 100
5-10	945	69	7.30	510	180	35.29
10-15	1,592	79	4.96	317	74	23.34
15-20	1,848	117	6.33	204	86	42.16
20-25	1,399	167	11.94	174	83	47.70
25-30	834	127	15.23	105	56	53.33
30-35	490	71	14.49	53	22	41.51
35-40	320	70	21.88	50	20	40.00
II						
5-10	164	8	4.88	643	119	18.51
10-15	434	11	2.53	461	104	22.56
15-20	1,056	32	3.03	275	76	27.64
20-25	1,560	95	6.09	176	56	31.82
25-30	1,525	132	8.66	108	43	39.81
30-35	1,223	160	13.08	59	24	40.68
35-40	940	182	19.36	44	21	47.73

by the late Dr. John Brownlee, then Medical Superintendent of the Belvidere Hospital, Glasgow, and consisted of particulars relating to 842 vaccinated and 29 unvaccinated males admitted to the hospital in 1900-1. Macdonell grouped the data in various ways thought to correspond to social gradings and tested association between social status and vaccination, and between social status and fatality by means of the tetrachoric  $\tau$ . Having regard to the probable errors of the computed coefficients, it appeared

that there was no sensible association between either social status and vaccination or between social status and fatality. Macdonell accordingly concluded that: "The Glasgow statistics do not go very far, but as far as they go they do not justify the statement: That the apparent protection of vaccination is due to the unvaccinated belonging to classes of lower status which have a far smaller power of resistance to the disease than the better-nourished classes of a higher social status in which the members are more generally vaccinated" (see Macdonell, *Biometrika*, Vol. I, p. 375 and Vol. II, p. 135).

As a statistician I should have liked to see a more ample discussion of this point, but the evidence tendered is sufficient to shift the burden of proof upon the shoulders of those who assert that such a table as the one I quoted can be explained away on these lines; this burden has never been discharged. So far as I have followed the controversial literature, it seems that to explain away the contrast resort is now usually had to accusations of conscious or unconscious bad faith. In its extreme form the argument is of this type. The reason why, for instance, in the Metropolitan Asylums Board's experience, the fatality-rate on children aged five to ten who had not been vaccinated is nearly four times as great as that upon children who had been vaccinated is because the allocation to the class vaccinated or unvaccinated is made to depend upon the issue of the illness. *Either*, it is supposed, no entry of vaccinal state is made in the hospital books until the result of the illness is known, in which case the bias of the recorder leads him always to give the benefit of the doubt as to whether a child had or had not been vaccinated against vaccination in a fatal case and for vaccination in a non-fatal case, *or*, if entries are made on admission, they are revised before publication in accordance with what happened to the child.

In considering this proposition we need not fly into a passion over the insult to our professional good faith, that would be to turn to the emotional atmosphere. It is sufficient to remark that in the first place it testifies to a lack of self-judgment and in the second to a strange conception of practical reasoning. Those who argue in this way are usually people who take an intense interest in the subject, who really believe that compulsory vaccination is a monstrous wrong and the whole modern doctrine

of immunization a mad folly. It is emotionally impossible for them to believe that others could be very little interested in the matter, far too little interested to lend themselves to the troublesome process of faking entries in hospital registers which the explanation of the statistics on anti-vaccinist lines requires. It is rather amusing to notice that one inherently plausible charge against the material accuracy of hospital records leads to precisely the opposite conclusion to that desired by the anti-vaccinist. In the course of a discussion at the Royal Statistical Society a few years ago, a medical speaker asserted that in making the differential diagnosis between smallpox and chickenpox, the vaccinal state was taken into account, and, if the patient had been vaccinated, the diagnosis of chickenpox was likely to be made. Now as the difficulty of diagnosis is as between chickenpox and *very mild* smallpox, the result of this bias—if it exists—must be to add to the *unvaccinated* category more than its share of very mild forms of illness. Therefore, if vaccination is a matter of indifference, we ought to find that the *fatality*-rate on unvaccinated patients with smallpox is less than on the vaccinated; which is just the contrary of what we do find. I fear this quite plausible suggestion of bias could only be helpful to the anti-vaccinists in respect of incidence-rates, which, for reasons already given, I do not consider a suitable basis for statistical argument.

The second defect in arguments of this kind is their constant violation of the law of parsimony or Occam's canon, viz. their rejection of a simple and sufficient for a more complicated and no more efficient explication of a set of facts. It is clearly easier and simpler to believe that if the fatality of smallpox in vaccinated persons of an age group is less than in unvaccinated persons of the same age group, vaccination is responsible than that some undisclosed differentiation other than vaccination is the cause, *unless it is a priori* utterly improbable that vaccination could have had anything to do with the business. There is a tale of an Eastern physician who had as he conceived discovered a specific for plague. He administered the remedy to ten tailors and to ten barbers. All the tailors recovered and all the barbers died; he thereupon entered in his memorandum book, "This remedy is with Allah's blessing sovereign for tailors but mortal for barbers." That story is mildly funny because we cannot conceive how a man's trade

could possibly influence the prognosis in plague. If the practice of the Metropolitan Asylums Board's hospitals had been to make the sign of the Cross on the pillow of every second smallpox patient, the most statistically significant data showing that the fatality in the cross-marked beds was much less than in the others would not, in this sceptical age, convince any physician that making the sign of the Cross affects the prognosis of smallpox. It is this principle which led very able men like Creighton to prefer a complex to a simple explanation; in so doing *they* did not violate the law of parsimony, to them the simple explanation was incredible. As I have already suggested, down to the discovery of the immunological affinity between variola and vaccinia, such an attitude was intellectually justifiable. The basis of vaccination was empirical in the strictest sense of the word and some very able people cannot act on an empirical basis. They must have a rational basis. But now, after the cross-immunity experiments of Copeman, Gordon, and others, it does seem to me that preference for the complex over the simple explanation is not a mark of intellectual superiority but fanaticism.

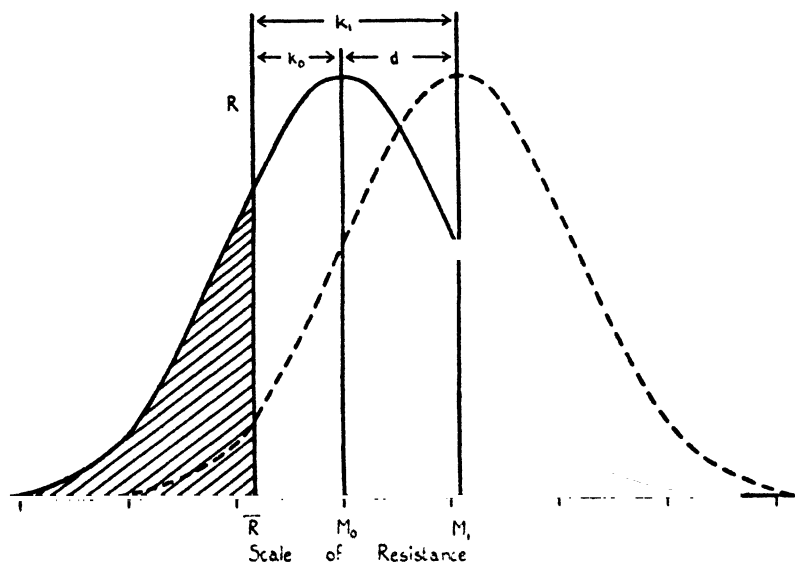
As Macaulay said, it is conceivable that Bishop Bonner burned the Protestant bishops because, knowing that the blood of martyrs is the seed of the Church, he was anxious to promote the interests of the Protestant schism; but ordinary people do not reason in that way, and it is, in my view, a pure waste of time to pursue these controversial paths. I accordingly turn to the question whether we can form any kind of estimate of the *amount* of protection conferred by vaccination against the risk of dying from smallpox when contracted. If we consider the reactions to any infection of individuals composing an ordinary population we may suppose that they vary continuously from extreme sensibility to extreme insensibility. In some cases, no doubt—that for instance, of an ordinary population exposed to the infection of pneumonic plague—the distribution is extremely skew, the proportion of the whole frequency capable of little resistance is very large; in others, perhaps acute poliomyelitis is an instance, the proportion of very refractory individuals is large.

But even in these cases we might conceive a dosage so small in the former and so large in the latter that the distribution of *reactions* (could these be measured) would not be highly asym-

metrical. It is therefore hypothetical—if the reader will, speculative—but not utterly unreasonable to think of natural resistance as a variable symmetrically disposed on either side of some unknown average value. If such a population were subject to an immunizing process, the easiest thinkable change is that the resistance of each member of it will be raised, that the resistance curve of the immunized will be similar to that of the unimmunized, but that the individuals will be symmetrically distributed around a mean resistance greater than that of the unimmunized. Again, this is not the *only* thinkable change. It might be that immunization has no effect at all on the very slightly (or the very highly) resistant, that the process operated not upon all but upon only a part of the treated population. But the hypothesis of an effect upon all is certainly the easier one to entertain. Assuming, then, this to be what happens, we must note that the fatality of an epidemic disease varies greatly from epidemic to epidemic and thus varies independently of the overt extent of immunization. Take for example the figures in Table 43 (page 283). The fatality on the vaccinated varied from nearly 10 per cent to only 1 per cent, that of the unvaccinated from more than 50 per cent to less than 13 per cent. We must therefore suppose that variations in the virulence of the *materies morbi*, of exposure, etc., are influential. Now let us imagine that the distributions of resistance in unimmunized and immunized populations are as shown in the diagram on page 281.

Along the base-line we suppose resistance to be scaled, and the ordinates of the curves measure the frequencies of individuals having a corresponding resistance; the scale of resistance runs from left to right, from the least to the most resistant. We suppose that in a particular epidemic all those whose resistance is less than that measured by the point R on the base-line die, i.e. the fractions of the areas of the two curves to the left of the vertical drawn through R and indicated by shading. The dotted curve symmetrically disposed about its mean is identical in shape with the full curve, but has its mean at a higher value of resistance. The verticals through  $M_0$  and  $M_1$  go through the means of the two curves. In this simple case, if we suppose that the curves take the particular form known as the Normal Curve of Error, then the result of a single epidemic would enable us to predict

how many vaccinated persons would die in an epidemic of any severity, the severity being measured by the mortality of the unvaccinated. Suppose, for instance, that it had been found in a particular epidemic that 20 per cent of unvaccinated attacked had died and 10 per cent of vaccinated attacked. One refers to a table of the Normal Curve (e.g. page 2 of *Tables for Statisticians and Biometricians*, Part I). The second column of this table,



GRAPH 4.

headed by the formula  $\frac{1}{2} (1 + a)$ , sets out the fraction of the area of the standard curve bounded by the ordinate drawn through the base-line at the point indicated by the  $x$  in the first column, this  $x$  being measured from the point marking the mean. Thus opposite  $x = 0$  we have 0.500000. The vertical through the mean point naturally divides the curve into two equal parts. If we look down the second column until we come to 0.8 in it we see that this does not appear, but as corresponding to the entry 0.7995458 we see  $x = 0.84$ , we may take that as the corresponding value, and, as the fractional area is at the left-hand end of the curve, we shall give it a negative sign and call it  $-0.84$ . Similarly corresponding to 0.9 we find for our  $x = -1.28$ . In other words, the mean of the resistance of vaccinated is  $+0.44$  "unit" from

the mean resistance of the unvaccinated, or 0.44 unit to the right of it (any difficulty will be removed by a glance at the diagram). If this is the "law," then knowing the mortality of the unvaccinated in any epidemic we can also determine that of the vaccinated. Suppose, for instance, that the mortality of the unvaccinated were 50 per cent. The equivalent  $x$  or deviation would be 0 and the corresponding deviation for vaccinated would be -0.44. Opposite 0.44 in the Table we find 0.6700314. In other words, 67 per cent of the vaccinated would survive and 33 per cent die. Had the mortality of the unvaccinated patients been 10 per cent, the equivalent deviation would be, as we have seen, -1.28; increasing this to -1.72, we find the corresponding value of  $\frac{1}{2}(1 + a)$  to be 0.9572838, or the mortality-rate on the vaccinated patients would be a little less than 4.3 per cent. The assumption that the frequency distribution of the immunized shall be identical with that of the unimmunized is, however, not only arbitrary but unnecessary.

Suppose, then, that although we still insist on the right-hand curve being of the same mathematical form as the left-hand one, i.e. still require that it shall be a "normal" curve, we permit it to be either more or less spread out than the left-hand curve; in other words, we do not require it to have the same standard deviation. In that case we could not solve the proposed problem from the data of a single epidemic, because instead of one unknown quantity we should have two. The deviations ( $x$ 's) of the tables are expressed in terms of the standard deviation, and we reached our result by considering the difference between -0.84 and -1.28, because each of these quantities is supposed to be a multiple of the same unit, viz. the standard deviation of the left-hand curve assumed to be the same as that of the right-hand one. In fact, putting it in symbols (see diagram) we had  $k_0 = k_1 + d$ , where  $k_0$  was -0.84 and  $k_1 = -1.28$ . But if the standard deviation of the right-hand curve were not equal to that of the left-hand one, but  $s$  times as large (where  $s$  may be greater or less than 1), then the -1.28 which we find in the Table is not  $k_1$  but  $k_1/s$ , which we may call  $a_1$ , and the equation becomes  $k_0 = a_1s + d$ . So that we have two unknowns  $s$  and  $d$  instead of  $d$  only. So another equation is necessary. For instance, suppose we had a second epidemic in which 30 per cent of the unvaccinated attacked

and 15 per cent of the vaccinated attacked died; then using the tables as described above we should have the pair of deviations  $-0.525$  and  $-1.04$ . Inserting these in the equation, we should have:

$$\begin{aligned}-0.84 &= -1.28s + d \\ -0.525 &= -1.04s + d\end{aligned}$$

giving  $s = 1.31$  and  $d = 0.8368$ , or  $k_0 - 1.31a_1 = 0.8368$ . We can use this equation to estimate the mortality of the vaccinated

TABLE 43

SMALLPOX EXPERIENCE IN PARTICULAR TOWNS

	Vaccinated			Unvaccinated		
	Attacked	Recovered	Per Cent	Attacked	Recovered	Per Cent
Sheffield, 1887-8 ..	4,151	3,951	95.18	552	278	50.36
Leicester, 1892-3 ..	199	197	99.00	158	139	87.97
Gloucester, 1895-6 ..	1,211	1,091	90.09	768	454	59.11
London, 1901 ..	1,166	1,051	90.14	354	241	68.08
London, 1902 ..	4,954	4,441	89.65	1,736	1,177	67.80
London, 1892-3 ..	1,539	1,503	97.66	370	285	77.03
Glasgow, 1900-1 ..	1,643	1,493	90.87	122	59	48.36
Bradford, 1893 ..	498	467	93.78	128	86	67.19
Manchester, 1892-3 ..	658	630	95.74	88	69	78.41
Batley, 1891-2 ..	347	338	97.41	167	121	72.46
Dewsbury, 1891-2 ..	135	130	96.30	119	87	73.11
Warrington, 1892-3 ..	586	548	93.52	68	44	64.71

from that of the unvaccinated (or the converse) just as before. To find the mortality of the unvaccinated when half the vaccinated die, we put  $k_0 = 0.0$ , giving  $1.31a_1 = 0.8368$  or  $a_1 = -0.64$ . Corresponding to  $x = 0.64$  in the table  $\frac{1}{2}(1 + a)$  is  $0.7389137$ , so rather more than 73 per cent of the vaccinated survive and rather less than 27 per cent die.

But why confine ourselves to two epidemics? If we do so, naturally we shall obtain an exact solution, since a straight line can always be drawn through two points, or using algebraical language a pair of independent equations in  $x$  or  $y$  will always give us values for the unknowns. If, however, we take more than two epidemics, i.e. have more than two independent relations

TABLE 44

	Proportions of Recoveries		Difference	Standard Error	Ratio of Difference to Standard Error
	Observed	Calculated			
Sheffield—					
Unvaccinated ..	0·5036	0·6026	-0·0990	0·02978	-3·32
Vaccinated ..	0·9518	0·9208	+0·0310	0·00535	+5·79
Leicester—					
Unvaccinated ..	0·8797	0·8805	-0·0008	0·03655	-0·02
Vaccinated ..	0·9900	0·9899	+0·0001	0·01000	+0·01
Gloucester—					
Unvaccinated ..	0·5911	0·5727	+0·0184	0·02517	+0·73
Vaccinated ..	0·9009	0·9089	-0·0080	0·01192	-0·67
London, 1901—					
Unvaccinated ..	0·6808	0·6199	+0·0609	0·03577	+1·70
Vaccinated ..	0·9014	0·9273	-0·0259	0·01158	-2·24
London, 1902—					
Unvaccinated ..	0·6780	0·6131	+0·0649	0·01620	+4·01
Vaccinated ..	0·8965	0·9247	-0·0282	0·00573	-4·93
London, 1892-3—					
Unvaccinated ..	0·7703	0·7853	-0·0150	0·03056	-0·49
Vaccinated ..	0·9766	0·9736	+0·0030	0·00562	+0·53
Glasgow—					
Unvaccinated ..	0·4836	0·5279	-0·0443	0·06395	-0·69
Vaccinated ..	0·9087	0·8890	+0·0197	0·01051	+1·87
Bradford—					
Unvaccinated ..	0·6719	0·6614	+0·0105	0·05892	+0·18
Vaccinated ..	0·9378	0·9413	-0·0035	0·01510	-0·23
Manchester—					
Unvaccinated ..	0·7841	0·7520	+0·0321	0·06358	+0·50
Vaccinated ..	0·9574	0·9662	-0·0088	0·01057	-0·83
Batley—					
Unvaccinated ..	0·7246	0·7570	-0·0336	0·04792	-0·70
Vaccinated ..	0·9741	0·9674	+0·0067	0·01279	+0·52
Dewsbury—					
Unvaccinated ..	0·7311	0·7348	-0·0037	0·05736	-0·06
Vaccinated ..	0·9630	0·9621	+0·0009	0·02311	+0·04
Warrington—					
Unvaccinated ..	0·6471	0·6450	+0·0021	0·08201	+0·03
Vaccinated ..	0·9352	0·9359	-0·0007	0·01435	-0·05

between the pair of unknowns, then we shall only obtain a unique solution if the relation between the unknowns is really a straight line relation.

We must, then, try to determine whether the relation of the unknowns is linear or approximately so, and, in the latter event, find the constants of the "best" fitting straight line. How this may be done is explained in a paper by Mr. Udny Yule and I in which the hypothesis here discussed (originally published by the late G. D. Maynard) is elaborated algebraically and arithmetically. Its application is illustrated by Tables 43 and 44.

The "best" equation connecting the normal deviations proved to be:

$$k_0 = 1.0059a_1 + 1.15868$$

So the mean resistance of the vaccinated is 1.16 units of the scale higher than that of the unvaccinated, and 87 per cent of the vaccinated have a resistance greater than the mean resistance of the unvaccinated, while only 12.3 per cent of the unvaccinated are more resistant than the mean of the vaccinated. Table 45 shows how far this hypothesis does reproduce the facts, or reported facts, when the equation is applied to data not used for its computation.

As will be seen, the fatalities predicted in this way often differ widely from those recorded—particularly glaring discrepancies have been collected at the foot of the Table. The widest divergences are mostly in the direction of overstatement, e.g. the fatality of smallpox in the unvaccinated patients of the Berlin Lazaretto in the epidemic of 1871-2 was recorded as 81.3 per cent, an enormous figure. Our equation predicts as the corresponding fatality for vaccinated 39.4 per cent, but the recorded figure is only 14.1 per cent. An anti-vaccinist might thereupon say that the explanation is deliberate understatement of the mortality in the vaccinated. But it is to be noticed that the advantage required even by the equation is a large one. Suppose we put the fatality of unmodified "classical" smallpox at the modest figure of 25 per cent; then, according to the equation, the vaccinated would experience a fatality of less than 4 per cent—that is, their chance of dying would be less than one-sixth that of the unvaccinated. If this way of measuring the facts approximates

TABLE 45

(For sources, see *Greenwood and Yule*,\* p. 27)

Data	Observed Fatality of Unvaccinated, Per Cent	Observed Fatality of Vaccinated, Per Cent	Calculated Fatality of Vaccinated, Per Cent
France, 1816-41 .. .. .	16.2	1.0	1.7
Marseilles, 1828 .. .. .	25.0	1.0	3.4
Württemberg, 1821-35 .. .. .	27.3	7.1	4.0
Württemberg, 1840-50 .. .. .	38.9	3.5	7.6
Canton Vaud, 1825-9 .. .. .	24.0	2.1	3.2
Bohemia, 1835-55 .. .. .	29.8	5.1	4.7
Milan, 1830-51 .. .. .	38.3	7.6	7.4
Verona, 1828-39 .. .. .	46.6	5.6	10.8
Copenhagen, 1828-37 .. .. .	27.6	1.0	4.1
Vienna Hospital, 1834 .. .. .	51.2	12.5	13.1
Vienna Hospital, 1837-56 .. .. .	30.0	5.0	4.7
Vienna Hospital, 1859 .. .. .	13.8	3.8	1.3
Vienna Hospital, 1870 .. .. .	17.4	2.0	1.9
Prague Children's Hospital, 1840-58 .. .. .	32.0	3.0	5.3
London Smallpox Hospital, 1836-56 .. .. .	35.0	7.0	6.3
London Smallpox Hospital, 1863 .. .. .	48.0	12.0	11.5
London Smallpox Hospital, 1864 .. .. .	36.0	8.7	6.6
London Smallpox Hospital, 1865 .. .. .	38.0	7.4	7.6
London Smallpox Hospital, 1866 .. .. .	35.7	7.3	6.5
London Smallpox Hospital, 1867 .. .. .	36.8	8.3	6.8
London Smallpox Hospital, 1868 .. .. .	34.0	6.2	5.9
London Smallpox Hospital, 1870 .. .. .	38.5	7.9	7.4
Frankfort Town, 1871 .. .. .	49.0	16.0	12.0
Coblentz, 1871 .. .. .	56.9	18.0	16.4
Quebec, 1819-20 .. .. .	27.0	1.7	3.9
Carniola, 1834-5 .. .. .	16.2	4.4	1.6
Carinthia, 1834-5 .. .. .	14.5	0.5	1.4
Adriatic, 1835 .. .. .	15.2	2.8	1.5
Galicia, 1836 .. .. .	23.5	5.1	3.1
Kiel, 1852-3 .. .. .	32.0	6.0	5.3
Malta (?) .. .. .	21.1	4.2	2.5
Epid. Soc. Returns .. .. .	23.0	2.9	3.0
Breslau, 1831-3 .. .. .	53.8	2.1	14.5
London Smallpox Hospital, 1871 .. .. .	66.5	14.9	23.3
Poland, 1871 .. .. .	33.0	11.4	5.6
Frankfort City, 1872 .. .. .	46.0	16.6	10.6
Frankfort and District, 1871 .. .. .	43.4	14.8	9.4
Liverpool Smallpox Hospital, 1870 .. .. .	72.0	12.7	28.4
Berlin Lazaretto, 1871-2 .. .. .	81.3	14.1	39.4
Lower Austria, 1835 .. .. .	25.8	11.5	3.6
Dalmatia, 1836 .. .. .	19.6	8.2	2.3
Illinois (?) .. .. .	48.6	6.1	11.8

at all to truth—as I think it does—the advantage of the vaccinated needs no commentary.

At this point our formal discussion of the subject—I use the word “formal,” not as we usually do in conversation, as equivalent to “trivial,” but rather as equivalent to “well-defined” or “exact”—must come to an end. I do consider that the data of fatality from smallpox are, with all their imperfections, sufficient to form a basis of a discussion conforming to the rules of statistical reasoning. I do not consider that data of incidence are sufficiently complete and comparable as between the vaccinated and unvaccinated to justify arithmetical analysis. I have, indeed, as an individual, almost as strong a conviction that recent vaccination is a thoroughly adequate defence against the risk of taking smallpox as anti-vaccinists have that it is worthless as a defence and otherwise pernicious, but I know of no data by means of which I could estimate the measure of such advantage even to the degree of approximation attained in the case of protection against death. In these circumstances it is perhaps impertinent to record my personal convictions at all, but if I refrained from doing so I should no doubt be claimed as a crypto-anti-vaccinist.

Some years ago, in the course of a discussion I said that there was a good deal of evidence in support of the proposition that Edward Jenner was a rogue—as indeed there is, and also a good deal (in my opinion, a good deal more) of evidence against it. I shall no doubt always be quoted by some fanatics as having said that Jenner *was* a rogue. Upon this subject I expounded my views even too copiously in the last chapter. I conclude this one by inferring from the statistical evidence which I have discussed that Jenner was, directly or indirectly, the means of saving many hundreds of thousands of lives. That is a less grandiose conclusion than some others have reached, yet, I submit, quite enough to entitle Englishmen to take pride in the recollection that Jenner was their countryman.

#### RECOMMENDATIONS FOR FURTHER STUDY

I should advise reading in the following order. First, Hirsch's article on smallpox, then Cumpston's *The History of Smallpox in Australia, 1788–1905*.

Next, Creighton's chapters on smallpox. Then Dr. J. C. McVail's

*Vaccination Vindicated* (1887), either followed or, if preferred, preceded by W. White's *The Story of a Great Delusion* (1885) and Creighton's *Jenner and Vaccination* (1889).

Then read Dr. Gordon's *Studies of the Viruses of Vaccinia and Variola* (1925. Medical Research Council's Special Report Series, No. 98). These works will, I think, give a pretty complete view of the facts as presented by the orthodox and the heterodox and of some other facts not known to the controversialists of the nineteenth century which are important.

To gain knowledge of the *present* position, the reader might begin with Dr. C. K. Millard's *The Vaccination Question in the Light of Modern Experience* (1914), then read the controversy between Dr. Millard and the late Dr. McVail in the *British Medical Journal* for 1919. Next, Dr. Ricardo Jorge's *Alastrim et Variole* (Lisbon, 1927).

Finally, the sections devoted to smallpox in the annual reports of the Chief Medical Officer of the Ministry of Health should be read.

## X

### PLAGUE

WE are all the dupes of words or of their emotional colour. One may easily demonstrate that in India in 1918 influenza destroyed in a few weeks far more lives than plague consumed in as many years, but the word "influenza" is emotionally colourless, while to all of us the mere name of that sickness which, scorning any adjectival qualification, is so emphatically *the* plague, brings a faint thrill.

Plague as an epidemic sickness can be traced in historical records further and more confidently backwards than any other named cause of death. There is no serious doubt that the sickness, beginning with "emerods [i.e. swellings] in their secret parts" which afflicted the Philistines after their capture of the ark of God, was bubonic plague, and there is very little doubt that this Near Eastern tribe had recognized *some* association between changes in the rat population and an epidemic sickness of man, for the trespass offering designed to propitiate the god of Israel consisted of "images of your emerods, and images of your mice that mar the land."\* Further East, folk-tales (as old as or older than those of the books of Samuel) linking up rodents and men by means of a sickness have been current. The inhabitants of villages on the Himalayan slopes knew ages ago that a mortality of or abnormal behaviour among rats or other rodents was a warning not to be disregarded.

Indeed, the story of plague might be material for a sermon to be preached on the text: "Because the foolishness of God is wiser than men; and the weakness of God is stronger than men." We shall see that it is a case, perhaps the only case, in epidemiology where the beliefs of unlearned people have contained far more essential truth and practical wisdom than the opinions of wise and learned men, even of men who survived into our own time.

Passing from pre-history to historical times, epidemics of plague meet us long before the Christian era. I do not, however, propose to go over the well-trodden ground of the pestilential constitution

\* 1 Samuel vi. 5.

of Thasos or of the Athenian plague, but to begin with the comparatively modern pandemic which spread through the Roman Empire in the time of Justinian from A.D. 542. To anticipate a little, it seems probable that endemic foci of rodent plague have existed in certain areas from time immemorial. One such focus is located on the west coast of Arabia, another in Uganda on the north-west bank of the Victoria Nyanza, another at the origin of the Euphrates and the Tigris. To one or other of these may be traced epidemics or pandemics making head in the Near East, in Africa, and, above all, in Egypt. From that source may be traced the Justinian plague. Further East lie the Central Asian and Northern Indian foci to which may ultimately be traced the outbreaks which seemed to begin in China, the two great pandemics of the fourteenth century and of our own age.

Between the three great pandemics—those of the sixth and fourteenth and the late nineteenth century—essential similarities are found in the leisurely progression, the vast mortality, and the gradual change from pandemicity to epidemicity. The differences are a less clear separation of clinical types, and in the latest manifestation a smaller general social disorganization and gross mortality.

It has been said, epigrammatically and therefore with exaggeration, that the plague of Justinian's reign broke up the ancient civilization and precipitated the "dark ages," that of the fourteenth century broke up the mediaeval system and precipitated "modern times." Careful modern historians have shown that this latter view at least is distorted, in that the economic reorganization was effected quite slowly. Still, it is not doubtful that the destruction of half the inhabitants of Western Europe in the course of two years did have a considerable effect on social organization.

The sixth-century pandemic extended gradually over Europe and did not reach these remote islands for many years. Its effects are matter of tradition; they were most felt in the epoch of struggle between the Celts and Saxons and lingered in folk memory as the plague of Cadwalader's time. By the fourteenth century epidemic plague was nothing but an old fairy tale to the inhabitants of Great Britain. The epidemiological history of the pandemic of 1347-50 can be traced with fair probability from

the Near East and conjecturally from South-western China. It is a fair conjecture that its ultimate source was the same as that of the pandemic of 1896, viz. changes in what, in our ignorance, we may call the balance of nature in the rodent population of the Gobi Desert area. That is no more than conjecture. The dissemination of plague from ships which carried the survivors of a siege in a Crimean *entrepôt* to South European ports is matter of fact. Where the fourteenth-century plague is said to differ from later experience is that in its quite slow extension across Europe it seemed to change as the season of the year changed from pneumonic to bubonic, and then from bubonic to pneumonic, without discontinuity. In the winter of 1347 the type was pneumonic at Avignon, which changed as the weather grew warmer to bubonic. When it reached England, probably first at Weymouth in the summer of 1348, it was probably bubonic, but London was involved in the spring of 1349, a time when in later experience plague was never epidemic there, and the epidemic may be set down as of pneumonic type. Later in that year the plague reached East England, where it wrought appalling havoc and was probably of bubonic type.

The subsequent history of plague in England illustrates the rule that a newly introduced disease at first prevails pandemically, then tends to limit itself to large aggregations of population. Pandemics occurred in 1361, 1368-9, 1371, 1375, 1390, 1405. But within a century of its reintroduction plague had become a disease of towns, and as London was much the largest town in England it was in London that its effects attracted most notice. In the sixteenth and seventeenth centuries London plagues occurred at irregular intervals of some ten years. The story ended almost like the dénouement of a novel, in a tremendous outburst in the years 1665-6. After 1666 plague did not regain a footing on British soil for two hundred and forty-three years, when it was again introduced and widely disseminated, but with results very different from those of 1348-9. The story of these events of our own time must sound trifling in comparison with those of 1665 or 1348, but it is instructive.

The scene of the incidents was a triangle in East Anglia having sides of some ten, ten, and eight miles, the eastern apex formed by the confluence of the rivers Stour and Orwell, the base by the

main line of the London and North Eastern Railway. The area is agricultural land dotted with a few small villages. To the north-west of it a few miles away lies the city of Ipswich, and a little to the north-east the seaside town of Felixstowe and some large villages.

In the winter of 1906-7 the headkeeper of Woolverston Park, a large estate here, noticed that the rats were dying in unusual numbers and that the corpses seemed well-nourished, but, the year being a dry one, nobody attached any special importance to the observation. Three miles east-south-east of Woolverston Park is the small village of Shotley. In December 1906 there was a cottage in Shotley occupied by a man of fifty-six, five women, and two children. All were alive and well on December 8th; by January 8th all had been attacked by and five had died of what passed for pneumonia. These occurrences may have been unconnected. But three years later a curiously virulent pneumonia invaded another household within two miles of the Shotley cottage, at Trimley across the Orwell. Here also were eight persons, of whom five died between December 22, 1909, and February 4, 1910. It was a very poor and—it is said—flea-infested cottage; father, mother, and five children (with a little girl on a visit) in two rooms. The mother first fell ill and she had a swelling the size of a small hen's egg at the angle of the jaw; so did a daughter, who sickened the day the mother died and herself died on January 5th. A younger sister who died five days later also had a swelling in the neck. The father, next to sicken, had a swelling in his groin which yielded no pus on incision and finally sloughed away. He recovered. The next incident was in the autumn in the village of Freston. A cottage housing two adults and five children was the scene. On September 12, 1910, a child was taken ill, died on September 16th, and was certified to have died of "gastric catarrh and pneumonia." The mother who had nursed the child was taken ill on September 21st and died on September 23rd; the certified cause of death was "septic pneumonia." On the day of his wife's funeral the husband fell ill; in three days he was dead and the cause of death was certified to be "influenza and pneumonia." On the same day a neighbour who had nursed the dead woman through the night of September 22nd-23rd died; her death was also ascribed to

"influenza and pneumonia." But the medical attendant was not satisfied; he gave a specimen of the sputum of the second patient in the series to a bacteriologist, who detected therein bacilli morphologically indistinguishable from *B. pestis*, while from the tissues of the third and fourth patients (blood and lung) bacilli were cultivated presenting the ordinary characters of *B. pestis*. Naturally these findings led to minute investigation. It was reported that rats and hares had been dying in the neighbourhood of the cottages, and a field survey made by C. J. Martin and the late Sidney Rowland revealed a wide distribution of plague; rat catchers brought them a bag of 568 rats taken over a wide area and 17 were plague-stricken; a series of infected foci was mapped out to the north-west of the triangle and one point was actually within it. Even ten miles away, on the land of the Labour Colony of the Woodbridge Union, of 35 trapped rats 5 were found infected.

So we reach this state of affairs in the autumn of 1910: four deaths from plague in man, plague-infected rats scattered over miles of country, and a presumption that five other deaths twelve months before and six deaths four years before had the same aetiology. The position changed little for several years. In 1911 plague-infected rats were found on twenty-seven farms distributed from Alderton on the north-east to East Bergholt on the south-west of the triangle. In that year one man, a seaman in Shotley barracks, died of plague. Year after year plague-infected rodents were discovered; in 1914 out of 500 examined 8 (3 ferrets, 1 rabbit, and 4 rats) were plague-stricken. But no other case of plague in man occurred until June 1918, when two neighbours resident in Erwarton (one and a half miles south of Shotley) died of plague. No case has been reported since and the plague in rodents has also, it seems, died out.

One has, then, presumptive evidence of rat plague in East Anglia from 1906 to 1918, direct evidence of its presence over a wide area from 1910; a probability that cases of plague in man occurred as early as 1906, proof that they occurred from 1910 to 1918. But plague did not establish itself, it never became an important cause of mortality in rats or men. One may surmise that the method of introduction was, on a small scale, similar to that which happened on a large scale in Bombay. There is,

or was, some grain trade between the Levant and the Orwell ports; presumably plague-infected rats came ashore and infection spread, spread widely. That a toll would be taken on human life like that of the Middle Ages or even that levied on the Indian peasants of to-day was not to be expected; the rat fauna is different, the habits of the peasantry are different, from those of modern India or of old England. Still, the travail might fairly have been expected to produce a more imposing mouse; not perhaps thousands but at least some scores of human cases. In plague, as in other sicknesses, something more is needed to generate an epidemic than even widespread and quite uncontrolled means of infection.

Returning to the larger scale history, it is to be noted that what happened in England in 1666 happened in France a little more than fifty years later. In 1720 the south of France suffered a frightful visitation of plague, and when that was over the plague epoch of France was closed. The same cycle was gone through a little later in Eastern Europe, and by the end of the eighteenth century even as far east as European Russia plague was no longer a socially important disease.

In the nineteenth century, apart from comparatively unimportant outbreaks in the Levant, North Africa and Egypt were the nearest territories at all seriously affected by plague. It is not quite true, but true enough for practical purposes, to say that in the nineteenth century plague was unimportant to Europeans, trivial in comparison with that other exotic Asiatic cholera.

The year 1896 was a year of fate for the world in more than one way. We might possibly hold that the Jameson Raid was the beginning, the first overt manifestation of enmities and forces which in due time were to overwhelm European civilization. Certainly the arrival of plague at Bombay was the opening of a fresh seal. It was the beginning of a new pandemic.

Before we consider what happened it will be as well to look through the cards sanitarians held when, in 1896, they sat down to play another game for high stakes. In what respect were they better equipped than the players in 1347 and in 1665? They knew that the *materies morbi* of plague was a bacillus (that discovery had been made a year before plague reached India) so that the miasmatic doctrine of ancient physicians could not mis-

lead them,\* but they knew no more than that. Indeed, the discovery may actually have done temporary harm, because people were set to track the dissemination of the germ, and at first they looked in all the wrong places. This new knowledge was offset by ignorance and contempt of old popular knowledge. It was not until too late that the primary importance of disease in rodents was thoroughly realized. In fact, in the game to be played, few good cards *were* held and none of them were played well.

The pandemic epoch which began in 1896 was preceded by events having a certain similarity to those of 1347. India herself (like Europe in the fourteenth century) had before experienced epidemics of plague. In the time of the Emperor Jehangir (the first quarter of the seventeenth century) plague appeared in the country districts of the Punjab, Lahore was infected and it reached Delhi. That this was *the* plague is indicated by a reference in a work by Nawab Mu'tamad Khan, the *Ikbāl-nama*, to a mortality of rodents. "When it was about to break out a mouse would rush out of its hole as if mad, and striking itself against the door and the walls of the house, would expire. If immediately after this signal the occupants left the house and went away into the jungle, their lives were saved: if otherwise the inhabitants of the whole village would be swept away by the hand of death."† Sir Thomas Roe's chaplain was present in Ahmedabad during the outbreak, but does not describe plague buboes. The Emperor Jehangir is, however, quite explicit: "Under the armpits, or in the groin, or below the throat a lump comes and they die." He

\* The Arabian physician known in Europe as Avicenna has been given the credit of perceiving the connection of the disease of rats with that of men, but with rather doubtful justification. Avicenna in his chapter on the premonitory signs of pestilence (*Liber Canonis*, Book 4, Fen. 1, Tract 4) begins with a merely traditional account of atmospheric corruption—fiery apparitions, shooting stars, turbidity of air, sun rising in mists, rapid multiplication of creatures bred from corruption, etc.—and adds: "*Et de eis quae significant illud est ut videas mures et animalia quae habitant sub terra fugere ad superficiem terrae et pati sedari commoveri hinc inde, sicut animalia ebria.*" The phrase I have italicized "gives the writer away." He is merely adopting the miasmatic theory of pestilence. Pestilence is due to a "miasma" rising from the earth, so, of course, creatures living in holes in the ground will first suffer and so one says they *do* suffer. The suggestion is not that he is recording a biological observation, but rather that he is asserting as a fact the consequence of an academic hypothesis. One did that in the days when faith in the all-sufficiency of human reason was greater than it is now.

† Quoted by Simpson, *A Treatise on Plague*, Cambridge, 1905, p. 41.

also records the precedent illness of rodents. This was early in the seventeenth century. Towards the end of the century, in 1684, plague was again epidemic in Western India. At the end of the century it disappeared almost as completely as in Western Europe. After more than a century of freedom, plague reappeared in Kutch, Kathiawar, Gujarat, and Sindh, continuing for eight or nine years, from 1812-21. Fifteen years later what was known as the Pali plague broke out in Marwar in Rajputana and lasted about two years. Finally there is some reason to suppose that at Garhwal and Kumaon on the southern slopes of the Himalayas plague had been endemic from at least 1823. As a whole, however, it may be said that in 1896 India had been free from plague for more than fifty years.

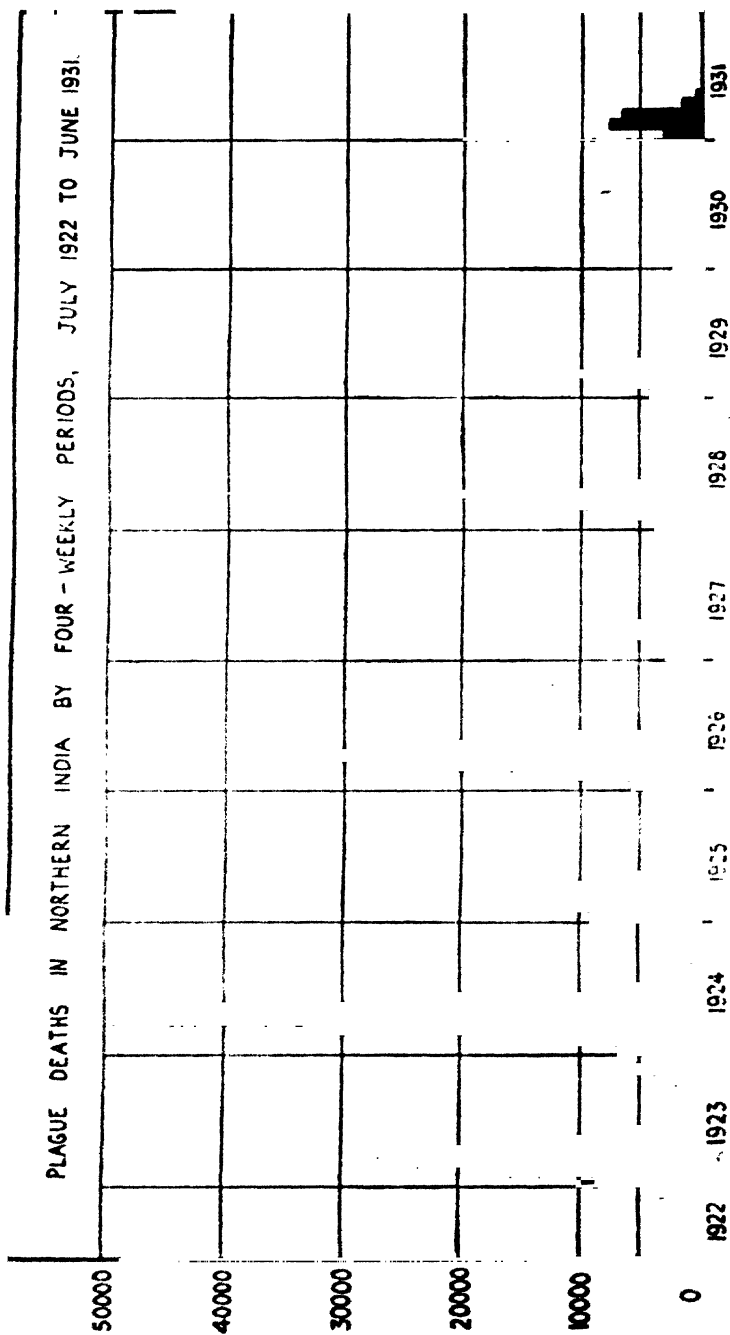
The events preceding the pandemic and relevant to it were these. The Chinese province of Yunnan at the eastern confines of Burma and Thibet has but limited intercourse with its neighbours. Such trade as it had was in the direction of Tonking. In 1871 plague of the bubonic form was epidemic in Yunnan and in 1882 plague was present in Pakhoi, a town through which goods from Yunnan usually passed (the usual route from the province was down the West River to Nanningfu and then overland to Pakhoi). Here and hereabouts plague continued to smoulder. When the Chinese authorities established a custom house in Mentgtze, in the south-east of Yunnan, plague was reported and there is no reason to doubt had been present some years before (the opening was in 1899); it is known that a severe epidemic occurred in 1892, and it was present in 1893 and 1894. These events only attracted local interest. But in 1894 the disease spread along the delta of the West River and Canton was involved. Canton was in direct communication with Yunnan by the West River, but prior to 1891 the route was not much used; in that year a change in local dues was introduced which made the river route more popular with merchants. Hong-Kong is in direct communication with Canton by river at a distance of only eighty miles and was soon involved (it was at Hong-Kong in 1894 that the plague bacillus was discovered independently by Kitasato and Yersin). Following the initial epidemic of 1894 (some three thousand deaths) plague was acclimatized in Hong-Kong. Between Hong-Kong and Bombay the volume of intercourse

is great. Bombay itself had had no plague for at least two hundred years. The epizootic had probably begun in Bombay as early as March 1896, the first human cases probably occurred in August and were not diagnosed. Rats were dying in large numbers but no notice was taken of the fact. It was not until the end of September that attention was directed to the probability that the disease was plague, and not until October 13th was the diagnosis bacteriologically established.

Even then no very drastic action was possible. The disease was mild and the population resented the activities of the public health department. In October and November the disease seemed to make little progress among human beings, but it was noticed that fresh infections were occurring, not in the districts from which people were fleeing, but in previously unaffected areas to which rats were migrating. Then almost suddenly at the beginning of December the mortality-rate doubled, continued to increase, and reached a maximum in the second and third weeks of February; in May it descended to the November level. Once the epidemic had set in the previously incredulous became panic stricken and there was an exodus from the city of almost half the population; with this exodus was associated a spread of plague beyond the city confines; the pandemic had begun. As five hundred and forty-eight years earlier, the rate of dissemination was slow; but it was sure. Writing in 1905, Simpson said, "Each year the area of its activity widens; each recurring epidemic seizes on new districts besides maintaining its hold on the old, and now at the end of eight years the annual mortality from plague in India has risen from less than 30,000 in the first year of its prevalence to little less than 1,000,000 per annum in 1903. This represents nearly one-sixth of the annual mortality of India."

In 1898 all the great provinces of India were affected, and in 1901 the toll of lives taken in the Punjab exceeded that in Bombay Presidency; in that year 217,910 died in Bombay Presidency, 221,767 in the Punjab.

The subsequent history can be traced in the admirably full and clear statements periodically made to the Local Government Board by the late Dr. Bruce Low. Sometimes the tide of mortality has ebbed, sometimes it has flowed, but indications that the sea is drying up are not wholly convincing. It is, however, a fact



GRAPH 5.

that since the war the movement has been favourable, as a graph prepared by the Health Organization of the League of Nations suggests (Graph 5).

There were only 23,825 deaths returned in 1930, the lowest total since the establishment of the pandemic, while the highest figure of the last ten years, 398,757, compares favourably with the 1,143,993 of 1904. The graph has some likeness to the trace of a pendulum movement upon a revolving drum, the swings gradually dying down. The post-1349 history is perhaps repeating itself.

As the seaboard of the whole world is mediately or immediately in communication with the Indian ports, it was to be expected that plague would be disseminated far and wide. Such was the case. In 1930 the recorded plague deaths of the whole world excluding Asia amounted to 5,888; all but 84 of these were in Africa, and of this tiny remnant 3 only were in Europe. This year was indeed a favourable one, but it may be said that, in spite of the wide dissemination, plague traceable to ship-borne infection has not since 1896 proved a serious factor of mortality either in Europe or in North America. In the African continent plague is still a serious cause of mortality, but only a small part of this is traceable to the Far Eastern developments of 1895-6.

During the thirty-eight years the present pandemic has endured, valuable additions to our knowledge of the epidemiology of plague have been made. The most important undoubtedly has been the discovery of the mechanism of transmission from rat to man. The hypothesis that a biting insect was the vector, dismissed contemptuously by the first official body to report on the situation after the involvement of India, was in a few years proved to be true, and ultimately the exact mechanism was brilliantly demonstrated by Bacot and Martin and much light has been thrown on the various biological factors concerned; but can we say that even now the epidemiology of plague is thoroughly understood? The answer is that we can say no such thing.

It is clear that in order that plague shall gain a foothold a host of conditions must be fulfilled the nature of which is unknown in detail. The work of the last thirty years has given us much general knowledge of the favouring or retarding factors, but as yet our knowledge is not sufficiently precise to enable us

to decipher the records and say why plague when introduced succeeds—as in 1348 or 1896—or fails—as in 1906-10—to establish itself.

Thus the importance of atmospheric, climatic, conditions in favouring or retarding the spread of plague has been considerably emphasized by work in India; climatic variations have been correlated with changes in the conditions of survivorship of both rat and flea. Then, again, the bionomics of rats and fleas, the local differences of distribution of the species of rat flea apt to transmit plague from rodents to man, have been carefully studied and—for instance in the recent work of Fabian Hirst—light has thus been thrown upon remarkable inter-local variations of incidence. One is gradually acquiring a detailed knowledge which in the end may lead up to a complete solution of the epidemiological problems. But we are still far from the end. I shall merely direct the reader's attention to some results of general observation which are of practical interest although they do not go very deep.

Given that a plague era is under observation, the following phenomena occur. Plague only manifests itself in heavily epidemic form when certain climatic conditions are present; it tends to be a strictly seasonal epidemic. Thus, in England—after the first bout—epidemic plague was restricted to the summer and early autumn; in the Punjab, heavy plague mortality is restricted to the months from the beginning of March to the end of June. In the off-season the disease smoulders amongst the rats, and the probability of its survival in a village or town increases with the size of the town. There may be, there certainly are, local peculiarities apart from mere size which favour the persistence of plague in a community, but speaking generally, infected villages become reinfected year by year from a small number of foci, as, perhaps, the world supply of plague is ultimately derived from but a few reservoirs. The probability that infection will reach a community increases with its size, other things being equal, and with its proximity to lines of transit, particularly lines of movement of human beings and human (cereal) food supplies. When plague does reach a community the amount of damage done depends upon, *inter alia*, the time of arrival in relation to the plague season—on the whole the later the date of entrance the less the mortality—and the size of the community—the smaller

the community the greater the rate of mortality *if it becomes infected*.

Tables 46, 47, and 48—samples of many that might have been quoted—illustrate the points.

TABLE 46

HOSHIARPUR

Month of First Infection	Total Population	Number of Deaths	Number of Villages	Death-rate per 1,000	Mortality Ratio (March = 1·00)	Mean Population of Villages
<i>Epidemic of 1905</i>						
December 1904 ..	71,162	3,534	98	49·66	1·59	726·14
January .. ..	194,770	6,495	230	33·35	1·07	846·83
February .. ..	87,999	2,391	119	27·17	0·87	739·49
March .. ..	82,962	2,585	144	31·16	1·00	576·13
April .. ..	96,801	2,640	186	27·27	0·88	520·44
May .. ..	49,109	977	96	19·89	0·64	511·55
June .. ..	29,774	423	65	14·21	0·46	458·06
July .. ..	6,664	86	14	12·91	0·41	476·00
Total ..	619,241	19,131	952	30·89	0·991	650·46
<i>Epidemic of 1907</i>						
December 1906 ..	73,603	2,475	99	33·63	1·14	743·46
January .. ..	119,808	3,346	123	27·93	0·95	974·05
February .. ..	96,984	3,069	139	31·64	1·06	697·73
March .. ..	133,924	3,937	224	29·40	1·00	597·88
April .. ..	113,387	2,248	192	19·83	0·67	590·56
May .. ..	39,691	569	90	14·34	0·49	441·01
June .. ..	18,463	108	20	5·85	0·20	923·15
July .. ..	2,748	15	5	5·46	0·19	549·60
Total ..	598,608	15,767	892	26·35	0·893	671·10

(Taken from *Journal of Hygiene*, Vol. XI (Supplement), December, 1911. 3rd Plague Report, M. Greenwood, Table XV, p. 110.)

The conclusions just stated are based upon statistical analysis of village plague and hardly rise above the level of description; they have, however, a certain practical importance. It seems to be probable that the maintenance of plague as a killing disease in a territory of scattered villages depends upon comparatively few foci, and that attention to these foci, to villages which bridge over the unfavourable season, may be a profitable measure of sanitation.

Passing now to a more intensive study of the immediate

epidemiological phenomena of a prevalence, the aetiology of the rise, decline, and fall of an epidemic curve, the work of the late John Brownlee, published in 1918 in a memoir not nearly so

TABLE 47

HOSHARPUR, 1907

Month of First Infection	Population	Number of Villages	Number of Deaths	Mortality, Per Cent	Average Population of Villages
<i>Infected villages having less than 1,000 population, showing month of first infection</i>					
December 1906	32,914	74	1,277	3·88	444·8
January ..	36,667	87	1,529	4·17	421·5
February ..	53,767	117	2,204	4·10	459·5
March ..	71,666	185	2,681	3·74	387·4
April ..	65,994	167	1,585	2·40	395·2
May ..	32,643	85	524	1·61	384·0
June ..	7,486	16	86	1·15	467·9
July ..	1,535	4	14	0·91	383·8
Total ..	302,672	735	9,900	3·27	411·8
<i>Infected villages having population over 1,000 and under 3,000, showing month of first infection</i>					
December 1906	40,689	25	1,198	2·94	1,627·6
January ..	43,073	29	1,054	2·45	1,485·3
February ..	28,723	19	865	3·01	1,511·7
March ..	62,258	39	1,256	2·02	1,596·4
April ..	40,908	24	663	1·62	1,704·5
May ..	7,048	5	45	0·64	1,409·6
June ..	3,945	2	13	0·33	1,972·5
July ..	1,213	1	1	0·08	1,213·0
Total ..	227,857	144	5,095	2·24	1,582·3

(M. Greenwood, op. cit., Table XXVI, p. 121.)

well known as it deserves to be, is much the most important contribution yet made to our knowledge. Brownlee showed that epidemics of plague, whether in men or rats, are nearly symmetrical, the constant  $\beta_1$  usually being quite small, but  $\beta_2$  nearly always differed significantly from 3.\*

\* Should any reader be unfamiliar with the elements of curve-fitting—*quod deus avortat*—he may be informed that in any symmetrical curve  $\beta_1$  must be equal to 0; in the particular symmetrical curve known as the "Normal Curve of Error"  $\beta_2$  must be equal to 3; while the larger  $\beta_2$ , the more highly peaked must the curve be; when  $\beta_2$  is small, the curve is flat-topped.

Brownlee made a thorough analysis of prevalences in rats as well as in men in Bombay (see Tables 49 and 50).

He pointed out that for both *M. rattus* and *M. decumanus* the

TABLE 48

GUJRAT, 1907

	Population	Deaths	Number of Villages	D.R.	Ratio	Average Population
<i>Villages infected in 2 months</i>						
Up to 1,000	81,009	8,476	224	10·46	2·24	361·6
1,000-3,000	31,925	1,495	24	4·68	—	1,330·2
<i>Villages infected in 3 months</i>						
Up to 1,000	107,763	12,424	232	11·53	1·16	464·5
1,000-3,000	72,732	7,238	51	9·95	—	1,426·1
<i>Villages infected in 4 months</i>						
Up to 1,000	49,097	6,316	93	12·86	1·17	427·9
1,000-3,000	43,800	4,811	27	10·98	—	1,622·2
<i>HOSHIARPUR, 1907</i>						
<i>Villages infected in 2 months</i>						
Up to 1,000	64,553	2,158	149	3·34	1·87	433·2
1,000-3,000	39,269	704	26	1·79	—	1,510·3
<i>Villages infected in 3 months</i>						
Up to 1,000	59,744	3,070	132	5·14	2·32	352·6
1,000-3,000	46,229	1,019	29	2·22	—	1,594·1
<i>Villages infected in 4 months</i>						
Up to 1,000	27,897	1,642	58	5·89	1·86	481·0
1,000-3,000	42,447	1,341	28	3·16	—	1,516·0

(M. Greenwood, op. cit., Table XXXV, p. 127.)

epidemics were symmetrical, but that their forms differed; in the brown rat the epidemics were more peaked,  $\beta_2$  was much larger for epidemics in brown than for those in black rats. He further noted: (1) that there was experimental evidence that a considerable proportion of the rat population at the end of an epizootic is still susceptible and inferred that not more than half the rat population was actually attacked in any epidemic; (2) that the average flea population harboured by a brown rat was twice

TABLE 49

SHOWING THE VALUES OF  $\beta_1$  AND  $\beta_2$  FOR EPIDEMICS OF PLAGUE IN MAN IN CERTAIN LARGE TOWNS

Town	Date	$\beta_1$	$\beta_2$	Town	Date	$\beta_1$	$\beta_2$
London ..	1563	0.119	3.222	Bombay ..	1898	0.014	3.433
London ..	1603	0.032	3.268	Bombay ..	1899	0.000	3.545
London ..	1625	0.022	3.727	Bombay ..	1900	0.006	2.723
London ..	1665	0.013	3.488	Bombay ..	1901	0.008	3.558
				Bombay ..	1902	0.221	2.910
Alexandria	1834	0.385	5.197	Bombay ..	1903	0.018	3.512
Alexandria	1840	0.212	3.418	Bombay ..	1904	0.112	3.808
Alexandria	1841	0.062	3.407	Bombay ..	1905	0.055	2.853
				Bombay ..	1906	0.010	4.402
Hong-Kong	1896	0.001	3.632	Bombay ..	1907	0.117	5.167
Hong-Kong	1898	0.334	4.387	Bombay ..	1908	0.296	4.926
Hong-Kong	1899	0.074	3.864	Bombay ..	1909	0.358	4.720
Hong-Kong	1900	0.153	3.855	Bombay ..	1910	0.043	3.059
Hong-Kong	1901	0.001	5.290	Bombay ..	1911	0.063	3.702
Hong-Kong	1902	0.016	4.051	Bombay ..	1912	0.016	4.102
Hong-Kong	1903	0.057	4.632	Bombay ..	1913	0.024	4.241
Hong-Kong	1904	0.001	3.515				
				Poonah ..	1897-8	0.007	3.691
Sydney ..	1900	0.001	3.356	Poonah ..	1899	0.395	4.709
				Poonah ..	1900-1	0.256	4.026
Lahore ..	1903	0.212	4.419	Poonah ..	1901-2	0.561	3.190
Lahore ..	1904	0.004	4.888	Poonah ..	1902-3	0.307	4.941
Lahore ..	1905	0.005	4.456	Poonah ..	1903-4	0.001	2.539
Lahore ..	1906	0.694	6.008	Poonah ..	1904-5	0.027	3.381
				Poonah ..	1906	0.077	4.373
Calcutta ..	1901	0.004	5.180	Poonah ..	1907-8	0.118	2.597
Calcutta ..	1902	0.014	4.507	Poonah ..	1908-9	0.243	3.153
Calcutta ..	1903	0.179	5.020				
Calcutta ..	1904	0.017	5.401	Belgaum ..	1897	0.453	3.859
Calcutta ..	1905	0.043	5.310	Belgaum ..	1898	0.070	3.420
Calcutta ..	1906	0.620	4.097	Belgaum ..	1899	0.032	4.194
Calcutta ..	1907	0.337	5.171	Belgaum ..	1900	0.084	6.044
Calcutta ..	1908	0.323	3.454	Belgaum ..	1901	0.017	4.227
Calcutta ..	1909	0.002	3.385	Belgaum ..	1902	0.567	4.563
				Belgaum ..	1903	0.001	4.017
Jhansi ..	1911	0.337	3.999	Belgaum ..	1904	0.097	3.827

(Taken from "Theory of Epidemiology and Plague," by John Brownlee, *Proc. Roy. Soc. Med.*, 1918, Vol. XI, Sect. Epidem., Table I, p. 92).

that upon a black rat. Taking these data into consideration, it was possible to explain *separately* the epidemic curves of plague

TABLE 50

SHOWING THE VALUES OF  $\beta_1$  AND  $\beta_2$  FOR THE DISTRICT EPIDEMICS OF PLAGUE IN BOMBAY IN "MUS RATTUS" AND "M. DECUMANUS" AND IN MAN, 1905-6

District	M. rattus				M. decumanus				Man						
	Number of Rats	$\beta_1$	$\beta_2$	Mean of Epi. demic <sup>a</sup>	$\sigma$	Number of Rats	$\beta_1$	$\beta_2$	Mean of Epi. demic <sup>a</sup>	$\sigma$	Num-ber of Deaths	$\beta_1$	$\beta_2$	Mean of Epi. demic <sup>a</sup>	$\sigma$
Fort North and South ..	342	-0.182	2.749	83	2.64	1,346	+0.005	2.848	68	2.50	332	-0.002	2.923	96	2.60
Mandvi ..	1,230	+0.102	2.726	85	2.90	2,058	+0.125	2.753	66	3.13	498	-0.004	3.762	97	2.38
Chakla ..	448	-0.003	2.858	81	2.21	1,407	+0.007	3.170	67	2.37	308	-0.181	4.898	100	2.04
Market ..	347	-0.051	5.168	87	1.56	1,117	-0.310	4.401	72	1.85	429	-0.051	4.872	101	2.12
Oomarkhadi ..	456	+0.702	3.867	77	2.67	1,720	+0.425	4.171	54	2.24	549	-0.001	3.051	94	2.17
Dongri ..	374	+0.883	4.103	92	2.34	835	+0.375	4.316	68	2.35	512	+0.041	3.259	99	2.51
Dhobi Talao ..	237	-0.014	3.170	83	2.19	1,473	+0.068	3.282	67	2.26	506	-0.011	3.163	97	2.18
Bhuleshwar ..	519	+0.020	3.501	80	2.27	1,766	-0.058	3.577	58	2.18	631	-0.002	3.511	98	2.11
Fanaswadi ..	995	+0.157	2.587	83	2.16	348	-0.003	2.310	72	2.27	434	-0.004	3.355	101	2.23
Khara Talao ..	243	+0.551	3.725	76	2.78	1,072	+0.739	4.471	55	2.61	316	+0.048	3.175	100	2.21
Khumbharwadi ..	242	-0.149	3.292	85	2.05	1,018	-0.001	4.054	71	2.30	356	-0.470	5.017	100	1.81
Khetwadi ..	54	-0.695	3.313	98	1.99	217	-0.220	3.297	84	1.83	263	+0.244	4.241	109	1.89
Whole City ..	—	0.070	3.159	—	2.53	—	0.038	3.499	—	2.45	—	0.010	4.402	—	—

\* The mean of the epidemic is expressed in days from the beginning of the year.

Correlation of figures in this Table:

*M. rattus* and *M. decumanus*

Date of Mean

$\beta_2$

Man and *M. decumanus*

0.837

Man and *M. rattus*

0.722

0.691

(John Brownlee, op. cit., Table III, p. 96.)

in black and brown rats by the simplest of hypotheses, viz. that the epidemic declined because the proportion of susceptibles left alive was insufficient to keep the epidemic going. But it was not possible to explain the two sets of facts *simultaneously*. In his words:

"The form of the epidemic among the brown rats closely corresponds to that shown in the diagram as being due to an infectivity per infected unit of 1.6, the value of  $\beta_1$  being in this case small, the value of  $\beta_2$  3.58—approximately that given by the observations, namely, 3.50—and the proportion of susceptible units left uninfected, 30 per cent of the original number, a number sufficiently close to the facts for all practical purposes. If it is now assumed that owing to inferior power of transmission of the disease a lower degree of infectivity exists among the black rats, and that the proportion of black rats affected is half that of the brown rats, the infectivity among the black rats must be in the neighbourhood of 1.2, which would satisfy the conditions, namely,  $\beta_1 = 0$ ,  $\beta_2 = 3.16$ , and the percentage left = 60. The epidemic in the black rat would, however, require to have a standard deviation in proportion to that of the brown rat of 8.4 to 3.2, whereas the actual values are respectively 2.53 and 2.45. Further, if the theory held, the epidemic in the black rat would culminate very much later than that in the brown, unless some other circumstance interfered to suddenly terminate the epizootic. But such a sudden termination of the epizootic implies great asymmetry, and the data are in direct opposition to the possibility of this great asymmetry."

Brownlee therefore concluded that the hypothesis must be wrong, and held that the epidemic ceased owing to a loss of infectivity of the infecting organism.

I do not wish to discuss this hypothesis, which indeed I do not really understand, but I think Brownlee's demonstration that an epidemic is a self-regulating phenomenon which *must* be capable of biological description—when we know enough biology—is convincing.

Another important contribution to the epidemiology of plague made by Brownlee relates not to the morphology of prevalences but to the apparent movement of the time of maximum. In his memoir will be found several diagrams which suggest that plague epidemics do not tend on the average to recur at the same time each year, but that the interval is longer than a solar year. Hence, since we know that massive infection requires certain atmospheric conditions, the precession may shift the point of emergence into

a period wholly unfavourable to epidemic manifestation. That might result in a small town—or in a large town where the epidemic has become restricted to a few rat colonies—in the extinction of plague altogether. The point is an important one.

Lastly, attempts have been made to relate—for the purposes of forecasting—variations of climatic factors and variations of severity of plague. Brownlee gave some attention to this in the memoir from which I have quoted, and Sir Leonard Rogers has recently published a study of all the available Indian data. It does not appear to me that the stochastic association of the variables is sufficiently stringent to afford hope that results of much practical value will be obtained, but the data are of interest and deserve study. In making a statistical study of plague epidemiology we must remember that our data are peculiarly imperfect. It is not only that the field of modern observation upon a large scale is of countries where precise medical-statistical records are difficult to gather, but still more that, epidemiologically speaking, human plague is a mere epi-phenomenon. Our desired object of study is not the human crowd at all, but the rat herd. The vital and medical statistics of the kingdom of rats are still mere fragments.

It is usual and practically convenient to give separate consideration to the epidemiology of primary pneumonic plague. By primary pneumonic plague we mean clinically an inflammation of the lungs which is not preceded by a blood infection traceable to some portal of entrance of the bacillus other than the lung. In our time a great epidemic of plague having this clinical feature occurred in Manchuria; it lasted from September 1910 to the following April and killed more than 50,000 people. Some epidemiologists hold that this sickness is epidemiologically wholly distinct from the bubonic type. They point out that, *inter alia*: (1) the sickness is communicable directly from man to man; (2) its seasonal incidence is in the winter instead of in the summer and autumn (in England), or the season before the great heat of summer (as in India).

In my opinion, no such absolute distinction can be maintained. It is quite clear that in the pandemic of 1347–9 both epidemiological types occurred, and a quite competent observer (de Chaulliac) actually noticed the change of type between winter

and summer. The very full data relating to the Manchurian epidemic (see Dr. Wu Lien-Teh's *Treatise on Pneumonic Plague*, published by the League of Nations in 1926) make it as certain as such things can be that the epidemic began in the infection of tarbagan hunters from the tarbagan. The price of skins had risen and a great number of inexperienced persons had been attracted into the tarbagan country. "The native Buriats and Mongols possessed ancient traditions and long experience, which taught them to kill the animals by shooting, so that they are able to judge whether their prey was healthy or not. A sick tarbagan would be sluggish or lame, and would be avoided by them. Parties notified one another of the infected spots so that they might leave them alone. . . . In the case of the Chinese it was different. The new-comers were usually raw and ignorant coolies from the villages of Shantung who had never seen a tarbagan in their lives. They knew no history and had never heard of plague among the animals. Hence they caught tarbagans indiscriminately with snares and even congratulated themselves when they saw a sluggish one."\* This is another illustration of the danger of ignoring local traditions. In the tarbagan country there is, according to Sticker, a folk tradition that long ago tarbagans were men, that they were changed from men into tarbagans by a god who had been irritated by their boastfulness, and the proof of this story, said the tellers, is this, that a sickness falls upon the tarbagans, and when this happens, if their human brothers approach them the sickness will be communicated to the men. It also appears that in the early stages of the epidemic bubonic forms occurred, as, indeed, is said usually to have happened in pneumonic outbreaks. Of course this does not mean that there is no mystery about pneumonic plague as an epidemiological phenomenon; there is much mystery. The reason why man-to-man infection does not occur in bubonic plague is that an infected man is either healed or dead before bacilli are numerous enough in his blood to make the latter a suitable means of supplying a flea with infective material. Man is, in comparison with the rat, very sensitive to plague; if his first line of defence is carried he has small chance of survival. Therefore we have to explain how either host or parasite is so modified that a form

\* Wu Lien-Teh, op. cit., p. 72.

of disease communicable from man to man, almost infallibly killing the host but allowing him to survive long enough to infect others, comes into existence. So far no satisfactory explanation has been proposed.

There is a sense in which plague is a satisfactory disease to write about. Its history can be easily traced; it is spectacular, and its biology has been studied and explained with wonderful success. Again, the most pessimistic can hardly doubt that, until European civilization completely disintegrates, no bubonic plague will ever again make the havoc it did five hundred or even three hundred years ago.

There is another sense in which the subject is unsatisfactory. In spite of all we have learned in detail, we can still answer the great questions no more successfully than our ancestors. We know no better than they did why pandemics occur, and so, I think, even for us there is some magic in the title *The Plague*, some sense of the fearful unknown.

#### RECOMMENDATIONS FOR FURTHER STUDY

The standard historical work is Vol. I of Sticker's *Abhandlungen aus der Seuchengeschichte und Seuchenlehre* (Giessen, 1908). The plague supplements of the *Journal of Hygiene*, which appeared from 1906 onwards, are mines of information respecting work done in India.

## XI

### EPIDEMIC DISEASES OF THE CENTRAL NERVOUS SYSTEM

IN our notification data we distinguish Cerebro-spinal Fever, Acute Poliomyelitis, Polio-encephalitis, and Encephalitis lethargica.

How far it is logical from a philosophical point of view to separate these categories, to speak of them as distinct "diseases," is a question which might be argued at any length. I shall not at present argue it at all, but without prejudice, as the lawyers say, refer to the epidemiological features of each real or conceptual group.

*Cerebro-spinal fever* was probably familiar to both Sydenham and Willis, and has been a reasonably well-known epidemic disease in Europe since the beginning of the nineteenth century. The first universally acknowledged epidemic in Europe occurred at Geneva in 1805. This was a smallish outbreak; there were thirty-three deaths, but the gross pathological anatomy was well described by Matthey, who noted the congestion of the meningeal vessels: "a gelatinous humour covering the brain was markedly tinged with blood. There was fluid in the ventricles. The choroid plexuses were of a deep red colour. The base of the brain was covered by yellow puriform matter with no obvious change in the underlying cerebral tissue. This exudation covered the optic chiasma and extended backwards towards the cerebellum, reaching for the space of an inch down the vertebral canal."

Since then we have never been free from outbreaks, which seem to occur in secular waves, 1805-15, 1837-50, 1854-75, 1876-86, 1896 to the present day. The first period was characterized largely by outbreaks among troops and corresponds to the epoch of the Napoleonic War. The second epidemic period seems to date from happenings in Spain at the period of the Carlist civil war, whence the disease was introduced into France (owing to the war in Spain there was considerable concentration of troops in the south-western district of France), and the distribution through France is consistent with the disease having been spread by troops moving from cantonment to cantonment.

The third period, from 1854, was characterized by appearance of the disease in Sweden, and in place of widely scattered foci there seemed a tendency to uniform spread. The whole of Germany was involved. In this period, too, the United States (then at war among themselves) first experienced the disease. The fourth period, dated by Hirsch from 1876, was an epoch of scattered and usually small prevalences. The fifth wave, dated by Osler from about 1896, was characterized by widely scattered but quite severe outbreaks, and for the first time really important outbreaks are recorded in the United Kingdom. The war years 1914-18 were associated with important prevalences.

What may be called the immediate epidemiology of cerebro-spinal fever has been excellently displayed by J. A. Glover.\* Glover describes the events in the Guards' Dépôt at Caterham. Here in a dépôt normally accommodating eight hundred soldiers large numbers of men were introduced for training and there resulted gross overcrowding. Systematic sampling of the throat flora was carried out, and it was found (1) not only was there an evident correlation between overcrowding and the proportion of carriers, but (2) that an increase in the proportion of carriers among non-contacts as well as contacts preceded the clinical epidemic. Thus in September-December the non-contact carrier-rate was 7·5 per cent, but, during the epidemic, non-contacts as well as contacts had rates of 34 per cent (this is based on the whole period of the epidemic); during January-February—the winter was a very severe one—the rates actually reached the figure of 72 per cent. It may in fact be said, as Arkwright urged, that the carrier-rate constitutes the epidemiological event, clinical cases being in a sense epiphenomena; the determination of the case is, it seems, a function of previous experience: no less than 65 per cent of the actual patients were in their first month of military service.

We might look at it in this way. A meningococcus carrier is a species of machine gun discharging infective droplets. The number of hits he will register depends on the distance of his targets. If his comrades are sufficiently spaced out, all the shots will miss; bring them nearer to him or—what comes to the same thing—bring in more room-mates and not only will the number

\* *Journ. R.A.M.C.*, 1918, Vol. XXX, p. 23.

of hits increase, but those successfully hit will in their turn become machine guns and the proportion of carriers will be increased by both factors. If, for instance, our machine gun registered only 1 per cent of hits in the unit of time, so that at the end of the first exposure in a group of one hundred to the machine gun only one was hit, then, bringing the new gun into action, we shall double the number of hits, and only a small fraction of them will be wasted by hitting those already carriers. The carrier-rate will almost double and will quite rapidly approach 100 per cent. This is a mere illustration and leaves much unexplained; I shall return to it later. A great deal of overcrowding can exist without the development of cerebro-spinal fever epidemics. *Why* do epidemics occur when they do? Military life and the generalization of military life in war-time naturally favour the process, but cerebro-spinal fever was already a sensible cause of death before the war (163 deaths in 1913) and has continued to be a relatively important cause long after the war (588 deaths in 1929 and 632 in 1930, no less than 1,440 in 1931). There is a *tertium quid*. What it may be we do not know.

*Acute poliomyelitis* as an epidemic disease, or at least as a clearly recognizable epidemic disease, has a shorter history than cerebro-spinal fever. Sweden and the United States of America have suffered much more severely than our own country, where indeed prevalences worthy to be called epidemics—in the popular sense of the word—are not older than 1897; while it is only from 1910 onwards that much attention has been attracted to the disease in Great Britain. In 1911 a severe outbreak occurred in Devonshire and Cornwall which was the subject of an excellent study by the late Dr. R. J. Reece. In all, 154 cases with 34 deaths were brought under notice; in one small village (Stoke Rivers) with a population of 119 persons in 18 houses (41 of the persons attended the local school), 36 cases of poliomyelitis occurred. Fourteen houses were invaded and in 11 more than 1 case occurred. In the eleven years from 1921 to 1931 inclusive, notified cases of poliomyelitis have varied from a minimum of 339 in 1931 to a maximum of 1,159 in 1926, in which year 176 deaths were registered. It is in connection with the prevalences of 1926 that most English discussion of the epidemiology arose, and in the annual report of the Chief Medical Officer of the Ministry

of Health for 1926 (pp. 84-108) is to be found the best general discussion of facts, a discussion to which little has been added since. Unlike cerebro-spinal fever, which is a cold weather disease, epidemic poliomyelitis tends to prevail in the late summer and early autumn. The maximum of the Devonshire and Cornwall epidemic of 1911 was in August, in one of the hottest summers on record. In 1926, 55 cases were notified in the first quarter of the year, 62 in the second, 479 in the third, and 563 in the fourth. The two weeks of greatest prevalence were that ending September 18th when 78 were notified and that ending October 30th when 79 were notified. Much public interest was aroused in connection with two groups of cases. The first of these affected a group of schools in Broadstairs. Including 2 cases in July and August, 74 were diagnosed (62 notified) and there were 7 deaths. The maximum incidence was between October 10th and 13th. The weather in early autumn 1926 was unusually dry and warm. On the advice of physicians consulted by the school authorities, the pupils were not sent home and fairly strict measures of segregation were adopted. Shortly after this, poliomyelitis appeared in a large boarding school in another part of England, viz. Uppingham. A boy in the school fell ill with signs and symptoms of the progressive type of paralysis on November 5th and died on November 8th. Within the previous fortnight 6 cases of high temperature, sore throat, and catarrh occurred in the school. On November 12th another paralytic case occurred, and the governing body decided to break up the school and not to reassemble it until after the Christmas holidays. Since the action taken here was the precise converse of that adopted on the advice of some well-known London physicians in the Broadstairs schools, which catered, like Uppingham, for the articulate middle and upper classes, it was inevitable that controversy should be aroused. Whether the protagonists of the Broadstairs method were justified in choosing a lay newspaper as the venue is, no doubt, itself a controversial issue.

Like most discussions, even in professional journals, this became incoherent, and, *inter alia*, the same experimental facts (those published by Topley and I) were used by both sides as telling in their favour. Thus the experience of our colonies of mice that the introduction of fresh, healthy stock was sufficient to keep

a droplet infection going indefinitely was used as an argument in favour of not breaking up a school but segregating it. On the other hand Topley's experience that if an infected herd were broken up into smaller groups before the epidemic had gathered way, then the aggregate mortality of the smaller groups was much less than that of an undivided herd, was used as an argument in favour of the Uppingham policy. In truth, knowledge in 1926 (and also in 1935) of the precise mechanism of infection within a herd was so scanty that the discussion could not but tend to be theoretical; competent observers differed widely in opinion. The reader will find illustrations in the papers by Collier\* and Walshe,† and the subsequent controversy between these authors.‡ I am only able to offer largely theoretical comments and will merely draw attention to some comparisons.

Lavinder, Freeman, and Frost,§ and Aycock and Eaton|| have provided valuable statistical evidence tending to the conclusion that, in comparison with the zymotic diseases, familial infection in poliomyelitis is of minor importance. In the first place Aycock and Eaton point out that if the interval after that of the primary case is taken as abscissa and the number of secondary cases as ordinate, in poliomyelitis the curve is J-shaped with a single maximum near the origin. On the other hand the curves of occurrence of scarlet fever and diphtheria are multi-modal. As in poliomyelitis there is a maximum at or about the origin, but large secondary maxima of the same order of magnitude occur later in time, at the seventh and fourteenth day.

In all three cases it is reasonable to suppose that the first maxima relate to cases having the same origin as the primary case, while the later maxima, based upon intra-familial infection, indicate the evolution of the process in the group. The lack of secondary maxima in the poliomyelitis data is then evidence against the evolution within the family or group being at all similar to that characterizing zymotic diseases.

If comparison is made between the attack-rates on susceptibles in houses containing children ill with the disease, one finds that

\* *Lancet*, 1927, Vol. I, p. 321, and *Brit. Med. Journ.*, 1927, Vol. I, p. 751.

† *Lancet*, 1927, Vol. I, p. 326, and *Brit. Med. Journ.*, 1927, Vol. II, p. 347.

‡ *Brit. Med. Journ.*, 1927, Vol. II, pp. 469 and 516.

§ *United States Public Health Service Bulletin*, 1918, No. 91.

|| *American Journal of Hygiene*, Vol. V, 1925, pp. 725-41.

although the ratio of "cases" to exposed to risk is large the attack-rate is small. Thus in the New York data analysed by Lavinder, Freeman, and Frost, in the age group 0-5 there were 7,837 cases and 10,540 susceptibles at risk, but of the latter only 335 or 3.18 per cent fell sick. In the age group 6-10 the figures were 874 cases, and of 4,575 susceptibles, 58 or 1.27 per cent fell sick. In the age group 11-20, the cases were 208, the susceptibles 4,994, and 10 or 0.2 per cent were attacked. It is, however, true that the attack-rates on the exposed susceptibles were considerably higher than on the whole child population of the city in the corresponding age groups; in fact the rates per 10,000 were: all children 0-5, 124.5; exposed children 318; 6-10, 20.8; 127.0; 11-20, 2.3; 20.0.

When these figures are compared with those for scarlet fever and diphtheria it is found that the secondary attack-rates are: 0-5, 2,410.0 for scarlet fever, 1,490.0 for diphtheria; 6-10, 2,570.0 and 1,550.0; 11-20, 970.0 and 690.0.

Similarly, the comparison of attack-rates on all children and exposed children brings out an enormous discrepancy. For scarlet fever (Providence, R.I. data) the rates were: 0-5, 93.1 and 2,410.0; 6-10, 115.4 and 2,570.0; 11-20, 24.8 and 970.0. For diphtheria, 0-5, 111.1 and 1,490.0; 6-10, 97.2 and 1,550.0; 11-20, 23.7 and 690.0.

NAWAB SALAH JUNG SHAHJAHAN

*Encephalitis lethargica*.—That the clinical forms connoted by the name Encephalitis lethargica had been seen by physicians long ago is as certain as that the same proposition can be affirmed with respect to the two previously discussed illnesses, cerebrospinal fever and acute poliomyelitis. Crookshank's paper\* contains abundant evidence of this. Whether, epidemiologically, Encephalitis lethargica is part of the "epidemic constitution" of influenza is another matter; that it is a part, is strongly urged in the paper of Crookshank just cited and by Sir William Hamer.† Their case is, briefly, as follows. As far back as our historical record extends, it has been found that illnesses associated with signs and symptoms of nervous disease tend to be associated with epidemics which can be identified with influenza. Sometimes these nervous diseases (the phrase "nervous disease" is inexact,

\* *Proc. Roy. Soc. Med.*, Sect. Hist. of Med., Vol. XII, 1919, pp. 1-21.

† See *Epidemiology Old and New*, pp. 54 et seq.

but avoids verbiage) precede, sometimes they follow, the outbreak of influenza, but—and this is the fundamental proposition—they are part of the “setting” of the epidemic; Hamer has christened them “trailers.”

This view has not been generally accepted, partly I think because it has not been understood. Crookshank and Hamer did not claim that *cases* of Encephalitis lethargica and *cases* of influenza were clinically identical. Hence the statement that “in their manner of invasion, symptomatology, courses, and complications, influenza and Encephalitis lethargica stand clinically apart; their histo-pathological lesions are quite distinct, and in their epidemic

TABLE 51

## ENCEPHALITIS LETHARGICA

*England and Wales*

	1919	1920	1921	1922	1923	1924	1925
Notifications ..	541	890	1,470	454	1,025	5,039	2,635
Deaths .. ..	294	480	729	339	531	1,407	1,372

	1926	1927	1928	1929	1930	1931
Notifications ..	2,267	1,615	1,308	1,036	735	651
Deaths .. ..	1,325	1,155	1,072	1,037	916	962

behaviour there are striking differences,”\* would probably have been accepted by both Dr. Crookshank and Sir William Hamer as correct, but they would not have considered it as making in any way against their contention. Indeed, had Encephalitis lethargica been clinically or even epidemiologically identical with what we know as influenza there would obviously have been no basis for discussion. The whole contention is that these very different forms of clinical illness (I use the plural because certainly Sir William Hamer would include cerebro-spinal fever and acute poliomyelitis in the influenzal “setting”) are not influenza but part of its setting. If somebody were to remark that the first scene on the battlements of Elsinore is an essential part of the

\* *Report of C.M.O., 1924, p. 78.*

drama of *Hamlet* (I remember that one of the "Baconians," I think it was Ignatius Donnelly, maintained that Francesco was a wholly unnecessary character, merely introduced to bring in the name of Francis Bacon), he would not be confuted by the fact that the Prince of Denmark does not appear in the scene at all.

It is, however, quite true that even if the first scene is no more than a part of the whole drama, it may be very well worth while

TABLE 52

DEATHS FROM ACUTE POLIOMYELITIS, ENCEPHALITIS LETHARGICA, AND  
CEREBRO-SPINAL FEVER FOR 1913-31

*England and Wales*

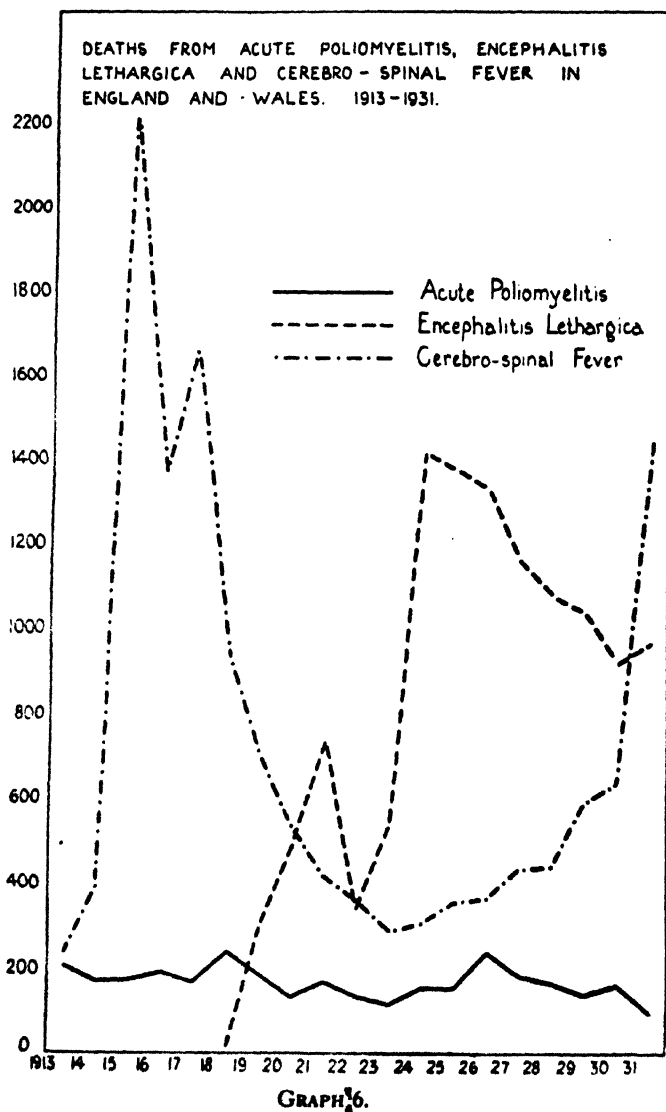
Year	Acute Poliomyelitis	Encephalitis Lethargica	Cerebro-spinal Fever
1913	206	—	232
1914	170	—	396
1915	172	—	2,203
1916	190	—	1,368
1917	168	—	1,651
1918	237	16	926
1919	183	294	694
1920	134	480	533
1921	169	729	416
1922	136	339	360
1923	119	531	284
1924	157	1,407	310
1925	156	1,372	354
1926	235	1,325	365
1927	182	1,155	430
1928	167	1,072	438
1929	140	1,037	588
1930	164	916	632
1931	98	962	1,440

studying it separately; in fact the actors who intend to sustain the characters *must* study it separately. Even if we accept the whole Crookshank-Hamer doctrine, it may still be well worth while to study the behaviour of Encephalitis lethargica as a crowd phenomenon *as if* it were unconnected with other epidemiological events. That is the pragmatic case for the orthodox practice.

From 1919 to 1931 the annual numbers of notifications and deaths were as in Table 51.

The peak year was 1924.

Poliomyelitis and polio-encephalitis culminated in 1918. Cere-



bro-spinal fever produced more deaths in 1931 than in any year since the war.

If we take the three sub-groups as a group and speak of them conveniently, if inaccurately, as epidemics of the nervous system, it appears that in the last decade no ground has been gained. In 1922 the group was responsible for 835 deaths, in 1931 for 2,500. This is, perhaps, an unfair comparison, but a study of Table 52 and Graph 6 shows that the trend is certainly not downwards.

My predilections favour the view that these illnesses *should* be regarded as, epidemiologically speaking, belonging to the influenza group, and it is not too pessimistic to say that this group offers the Achilles heel of our epidemiological body. If, owing to social and economic changes, civilization has to pass through another period of social disorganization at all comparable with that of the sixth century or the early seventeenth century in Germany, it may be that influenza and its associates, rather than typhus or plague, will reap the harvest.

#### RECOMMENDATIONS FOR FURTHER STUDY

*Epidemic Diseases of the Central Nervous System*, A. S. MacNalty. Second Edition. 1932.

*Poliomyelitis: A Survey*. Various authors. Baltimore (Williams & Wilkins). 1932.

## XII

### INFLUENZA

I SAID that the story of typhoid was a good beginning for the part of my book devoted to the special epidemiology of acute diseases because the success of our application of knowledge respecting its epidemiology had been great. Influenza is a good topic with which to end a discussion of the acutely epidemic diseases because our failure—whether to perceive the significance of what we know or to know what is significant—has been complete, and one should end any instruction with an appeal for further study.

In most instances, in all which I have discussed, modern epidemiological investigation has been helped or, some would say, hampered by a sufficiently vivid picture of the typical "case" of sickness, the prevalence of which was to be studied. That remark does not apply at all to influenza. The use of the term in medical practice is precisely in accordance with the method a cynical naturalist once gave me of distinguishing between crows and rooks: "If you see three or more they are rooks, if only one or two they *may* be crows." The practical definition of influenza is therefore purely epidemiological, and amounts to this: an apparently sudden disturbance of the public health by the occurrence of a very large number of cases of illness characterized as regards a majority by signs and symptoms affecting the respiratory system. Unphilosophical and incomplete as is this definition, it is sufficient to enable us to track down epidemics of influenza without difficulty through more than two hundred and fifty years. There is not much uncertainty about the identifications through another century backwards in time. There is still not complete unanimity as to the epidemiological nature of the much discussed sixteenth-century epidemics known as the English Sweats, but the arguments of Sir William Hamer and the late Dr. Crookshank have certainly satisfied me that these outbreaks properly come under the connotation of influenza. This matter is not of merely archaeological interest; the researches of the epidemiologists I have

mentioned have demonstrated that, in spite of the seeming spontaneity of an actual epidemic, there is reason to look upon the epidemic as but one link in a chain of epidemiological happenings. In particular, even the study of purely objective annals, such as those of Huxham in the first half of the eighteenth century, brings out a curious clustering of "nervous" and "intermittent" fevers around epochs of explosive influenza. In the previous chapter I briefly referred to the work of Crookshank and Hamer on this subject; here it must suffice to reiterate that the actual epidemic cannot possibly be understood as an isolated phenomenon. No doubt that remark applies in strictness to *every* epidemiological event. We treat an epidemic of typhoid, the Worthing outbreak or the Maidstone outbreak, as an isolated event, and seek for its immediate aetiology in a particular distribution of infective material. We may fairly be asked whether it is certain that the impugned water supplies had never before become contaminated, and, if they had, why on *this* occasion but not on a previous one, the epidemic became overt. There, too, it may be logically and fairly urged, were precursors, a setting of the epidemic worthy of examination.

Those submissions are logical: we have seen that some great epidemiologists, such as Pettenkofer, have attached considerable importance to them. We have also seen that a myopic view of the facts, an almost exclusive attention to immediate phenomena, and hand-to-mouth aetiology have in the typhoid group had pragmatic justification. Perhaps we may even say that there the immediate precursors are of more importance than the larger general factors determining a setting. In the study of influenza we have no such pragmatic justification, and so may entertain the hypothesis that here the factors determining the setting, factors which we do not understand, are more important than the particular factors which we can unmask. Those are, indeed, the reasons why epidemiologists have thought of influenza as the arcanum of their study, and have spoken of terrestrial or even cosmic determinants. I do not intend to discuss any of these cosmic hypotheses, because I do not know the meaning of the variates proposed for study nor how to measure them. Sir Francis Galton in the first number of *Biometrika* told the story of how one hundred and twenty years ago some earnest young students



of geology approached the despotic President of the Royal Society with a request to be allowed to circulate, under official sanction, a series of questions. Sir Joseph Banks was not in a conciliatory mood, and dismissed the deputation with the apothegm that a few fools could ask more questions in half an hour than wise men might answer in years. I am as far from thinking that the originators of cosmic theories are fools as from believing that statistical investigation and wisdom are synonyms. Indeed I am, emotionally, confident that the general aetiology of influenza cannot be displayed by the statistical analysis of the immediate epidemic phenomena. I am equally confident that we shall make no further progress through the jungle towards the palace of the Sleeping Beauty until we have by means of the experimental-statistical methods described in Part I gained more insight into problems akin to those of influenza, but simpler and still unsolved. In what follows I shall confine myself to the mere description of *some* of the phenomena, having warned the reader as clearly as I can that this is only a part of the truth. Within the statistical age, i.e. since 1837, the overt influenzal period falls into five stages. The first was brought to an end by a very severe epidemic in the years 1847 and 1848. There followed (in England and Wales) an interpandemic period from 1849 to 1889. Then there was a pandemic, followed by another interpandemic period brought to an end in 1918-19. We are now in an interpandemic period.

Table 53 shows some significant facts. The columns after the first show death-rates at ages in what I will call the first epidemic period, the first interpandemic period shown in two stages, the second pandemic period, the second interpandemic period in two stages, the third interpandemic period. The third pandemic period cannot be shown, for it was at a time when, owing to war service of a large proportion of the population, rates of mortality at ages cannot be computed with sufficient accuracy.

In Table 54 the rates are expressed as percentages of the rate at 0-5 years. This method of comparison for the purpose in view is better than the confrontation of the rates, because, owing to changes of nomenclature and classification, the rates themselves are not strictly comparable. We see that between the first pandemic, 1847-48, and first interpandemic period there is very little change of age distribution; both curves are U-shaped,

TABLE 54  
DEATH-RATE PER 1,000,000 FROM INFLUENZA (PERSONS)  
*England and Wales Expressed as Percentages of the Rates at Ages 0-5*

Age	1847-8	1848-72	1881-90	1890-1	1891-1900	1901-10	1911-7	1927
0-	100	100	100	100	100	100	100	100
5-	11	9	15	18	17	19	16	13
10-	7	5	12	15	14	15	12	9
15-	7	6	27	38	34	33	26	19
25-	11	8	46	64	52	53	41	30
35-	19	13	73	113	98	91	66	41
45-	40	28	104	194	171	164	95	48
55-	113	84	173	346	352	357	184	93
65-	333	295	319	649	769	823	428	149
75-	773	740	735	1,096	1,633	1,818	949	250
85-	1,577	1,219		1,575				

the limb of the U to the right being much the longer. In the second pandemic epoch, 1890-91, the right-hand limb of the U is much exaggerated, while the connecting limb is raised. In the second interpandemic period the accentuation of the right-hand limb of the U is increased. In the third interpandemic period, the present time, there is still a U, but the right-hand limb has been very much reduced in length. In the third pandemic period this relative depression of the right-hand limb went much farther, although its precise description is impossible. The following argument is a sufficiently exact demonstration. If, in the County of London, the death-rates at ages from influenza had borne, one to another, the same ratios as in 1913, but had been each increased to an amount necessary to provide the gross mortality, then—assuming that the age distribution in 1918 was the same as in 1921—the following distribution would have been obtained:

TABLE 55

## DEATHS FROM INFLUENZA

Age Group	Expected	Observed
0-5	815	1,493
5-20	499	2,067
20-45	2,002	5,890
45-65	3,886	2,220
65-	6,680	1,216

The great excess of deaths in early and early-middle life is plain, and the method of calculation probably understates the facts, for it is likely that in 1918 the proportion of the young in London was less than in 1921. In other words, there was a very remarkable shortening of the limbs of the U and elevation of the cross-bar. This change was, as Dr. Stevenson showed, quite abrupt. The age distribution of deaths from influenza right down to the emergence of the first wave of the pandemic in the summer of 1918 was perfectly normal.

The changed age distribution was still dramatically in evidence in the third wave of the pandemic, that of the winter of 1918-19, but not so much as in the previous wave. Since the pandemic there has been, as the Table shows, a reversion towards the pre-

viously normal type, but not by any means a complete return to the *status quo ante*.

There is then no doubt at all that in one important respect the influenza of 1918-19 was unprecedented within the period of statistically characterized experience. Whether it were *absolutely* without precedent is not a question we can answer confidently. It is a pity that the contemporary recorders of the Sweats were—like Caius—not much interested in age distribution, for there is at least a suggestion that the Sweat fell heavily upon the young.

The other respect in which the influenza of 1918-19 was unprecedented was, of course, the havoc it wrought. We should need to go back to the pestilence of 1348-9 for anything certainly more impressive, and there is some psychological interest in the fact, which most readers are old enough to recollect, that actually the emotional impression created was fainter than that produced by much less grave epidemiological happenings.

Although this pestilence caught us preoccupied by war, and unable to record happenings with normal precision, many data were collected. English experience is recorded in the statistical report issued by the General Register Office and the general report prepared in the Medical Department of the Ministry of Health.

As one of the compilers of the latter report, I am not an impartial critic of it, and my judgment of it must be accepted with the necessary caution. I think, then, that our conclusion that domestic overcrowding was not a sensible factor of the spread of influenza has not been invalidated by any subsequent discovery. Our conclusion that, while the passage through an attack of influenza on the average increased immunity from subsequent attack, the rule was subject to numerous exceptions, also seems to stand the test of time (see Tables 56-58). Our surmise that recurrences of epidemic influenza of serious magnitude and, in respect of age distribution, falling between the 1918 and pre-1918 type, were to be expected, and that influenza would continue to be a serious matter, has, unfortunately, been completely verified.

In the ten years since the pandemic the number of deaths assigned to influenza has been every year much greater than in the decennium before the war, and in the years 1922, 1927, 1929 has so far exceeded the average as to justify the term epidemic.

# INFLUENZA

327

TABLE 56

SUMMER AND WINTER

	(1) Total Investigated	(2) Per Cent Attacked amongst those previously Attacked	(3) Per Cent Attacked amongst those not previously Attacked	(4) Probable Error of the Difference (2) and (3)
South Shields .. ..	462	7.1	7.6	$\pm 4.84$
Leicester .. ..	4,619	7.4	8.4	$\pm 1.07$
Wigan .. ..	1,075	2.2	11.6	$\pm 2.93$
Newcastle .. ..	4,461	14.8	8.2	$\pm 1.17$
Manchester .. ..	4,686	4.1	2.1	$\pm 0.42$
Blackburn .. ..	1,284	6.3	7.9	$\pm 1.79$
Widnes .. ..	3,417	5.0	11.6	$\pm 1.09$
Cambridge University..	1,766	5.9	12.5	$\pm 1.17$
City of London Police ..	746	0	4.2	$\pm 1.91$
Clifton .. ..	451	51.9	50.5	$\pm 3.31$
Haileybury .. ..	515	17.8	39.1	$\pm 2.90$
Finchley School ..	1,224	3.7	3.0	$\pm 1.70$

(Taken from Report on Pandemic of Influenza, 1918-19, M.O.H., Table 3, p. 141.)

TABLE 57

AUTUMN AND WINTER

	(1) Total Investigated	(2) Per Cent Attacked amongst those previously Attacked	(3) Per Cent Attacked amongst those not previously Attacked	(4) Probable Error of the Difference (2) and (3)
South Shields .. ..	462	10.7	7.5	$\pm 3.48$
Leicester .. ..	4,619	5.8	8.8	$\pm 0.78$
Wigan .. ..	1,075	3.7	11.8	$\pm 2.44$
Newcastle .. ..	4,461	8.3	8.6	$\pm 1.28$
Manchester .. ..	4,686	3.0	2.3	$\pm 0.50$
Blackburn .. ..	1,284	12.2	7.5	$\pm 1.98$
Widnes .. ..	3,417	2.8	11.5	$\pm 1.29$
Cambridge University..	1,766	10.3	11.1	$\pm 1.15$
City of London Police ..	746	4.3	3.8	$\pm 1.31$
Clifton .. ..	451	61.2	47.3	$\pm 4.99$
Haileybury .. ..	515	30.7	31.9	$\pm 3.33$
Finchley School ..	1,224	1.0	4.2	$\pm 0.71$

(Op. cit., Table 4, p. 142.)

TABLE 58

SUMMER AND AUTUMN

	(1) Total Investigated	(2) Per Cent Attacked amongst those previously Attacked	(3) Per Cent Attacked amongst those not previously Attacked	(4) Probable Error of the Difference (2) and (3)
South Shields .. ..	462	7.1	6.0	$\pm 4.37$
Leicester .. ..	4,619	4.9	15.4	$\pm 1.37$
Wigan .. ..	1,075	2.2	7.9	$\pm 2.73$
Newcastle .. ..	4,461	1.4	5.4	$\pm 0.92$
Manchester .. ..	4,686	9.9	10.1	$\pm 0.83$
Blackburn .. ..	1,284	7.2	7.9	$\pm 1.71$
Widnes .. ..	3,417	3.3	9.2	$\pm 0.97$
Cambridge University..	1,766	9.7	30.2	$\pm 1.58$
City of London Police ..	746	8.0	16.2	$\pm 3.59$
Clifton .. ..	451	13.6	34.3	$\pm 2.93$
Haileybury .. ..	515	22.8	21.8	$\pm 2.59$
Eton .. ..	753	7.4	47.8	$\pm 2.18$
Harrow .. ..	429	32.0	76.1	$\pm 3.76$
Finchley School ..	1,224	13.4	35.5	$\pm 2.91$

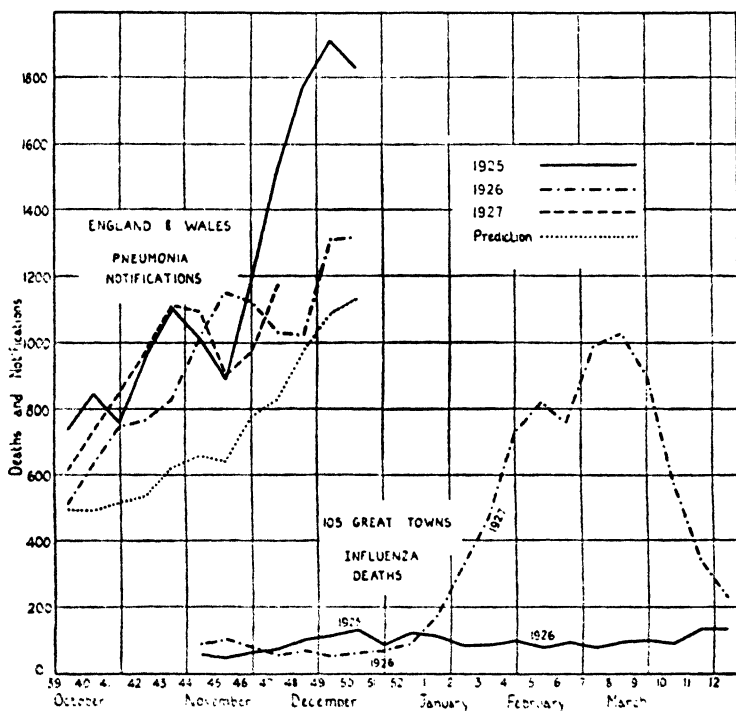
(Op. cit., Table 5, p. 143.)

The most recent of these experiences, that of 1928-29, has been in some respects the most severe, although falling far short of the severity of the pandemic.

In consequence of our experience in 1918-19, an attempt has been made to increase our means of information by making primary pneumonia a compulsorily notifiable disease.

It will be useful here to consider how far the information so made available has been of service. Graph 7 brings into relation the alleged incidence of pneumonia and other evidence of prevalence of influenza. It is advisable to explain first the routine practice of the Medical Department of the Ministry of Health as to the weekly recording of epidemic prevalences. For the numerically important notifiable diseases, viz. scarlet fever, diphtheria, and pneumonia, an ideal or "normal" graph is prepared which shows the absolute incidence of cases both for the whole country and for London separately for each week of the year. For scarlet fever, diphtheria, and pneumonia

we base this upon the previous nine years' experience, and we have, after trial of different averages, adopted the median as the most satisfactory statistical constant for the standard or norm. Each Thursday the actual notifications of the previous week are received, and in the report transmitted to the Ministry on the Friday the



indeed, clear proof that, as a recorded cause, pneumonia has been generally increasing and has often a prevalence far above the computed norm without mortality from influenza becoming serious. In other words, it has not been our experience that notified pneumonia is at all a certain pointer to the emergence of epidemic influenza; we cannot, in fact, justly claim that we are really in a much better position to forecast epidemic influenza or to estimate its probable duration or importance than we were before.

We cannot even say that foreign advices have been reliable means of forecasting. The late epidemic was, indeed, preceded in England by widespread prevalence in America. But in 1921 the prevalence in America was so serious that it was thought right to issue a warning here of the probability of a grave epidemic. In fact, although there was undoubtedly a minor epidemic, its scale was not impressive. When an epidemic has *begun*, it has often been possible to estimate fairly well the total mortality and date of maximum from an analysis of the rate of increase. Even these humbler ambitions are not always satisfied. Influenza affords hardly more satisfaction to the vanity of a statistician than to the feelings of a patient.

#### RECOMMENDATIONS FOR FURTHER STUDY

The Ministry of Health's report on the Pandemic of 1918-19 should be read; also a volume of studies edited by the late Dr. F. G. Crookshank and containing contributions from himself and Sir William Hamer (*Influenza: Essays by several authors*, London, 1922); finally, Sir William Hamer's *Epidemiology Old and New*, London, 1928, pp. 32-69.

For records of the havoc wrought, consult the official statistics of any country.

## XIII

### VENEREAL DISEASES

OUR present object of study differs in one essential respect from any of its predecessors. As before, we are, biologically speaking, concerned with acute infectious processes; but in all the previous examples although individual instances of infection occurred (sporadic cases which were clinically rather than epidemiologically interesting), large prevalences at particular times, what the man in the street calls epidemics, formed a subject of *primary* interest. In that sense none of the venereal diseases is an epidemic disease at all in North America or Western Europe. We have to do with prevalences, very large prevalences, which are not concentrated within narrow limits of time. Four centuries ago that statement would not have been correct. The behaviour of syphilis in Europe at the beginning of the sixteenth century was not greatly different, from the crowd point of view, from the behaviour of, say, influenza in 1918-19. Now, however, it is essentially different. Without entering upon the special peculiarities of the venereal diseases, it may be said that the change is similar to what has been observed in other widely prevalent crowd-sicknesses, such as tuberculosis. Whether at the beginning of the sixteenth century syphilis were really a "new disease" is an archaeological question I do not mean to discuss. At any rate, it then became more noticeable and widespread than in previous generations; it behaved *like* a newly introduced disease, like tuberculosis among aborigines who had had no previous experience of the white man's plague, or like measles. In that generation it was a killing disease. Within a century this rapid killing power was abated, but the evidence of surgeons in the Elizabethan age shows that the clinical manifestations of syphilis were more serious than those observed, say, at the beginning of the nineteenth century. One notices how the great pox gradually ceases in popular estimation to be an object of mortal terror, and becomes what it still is, an unpleasant but not capital penalty for breaking a taboo. Clinical writings on syphilis from the time of the early sixteenth-century epidemics are evidence of a change of type. We have no good English account of

the signs and symptoms in the pandemic, but numerous continental writers have made it clear that in its earliest form syphilis differed from what we know mainly in the extreme severity of the secondary stage—in our classification. The skin eruption and the inflammatory changes of mucous surfaces progressed far beyond anything we ever see now, and death, which was a frequent event, seems to have been due to a general septic infection, or to actual neglect, sick persons covered with stinking, purulent sores being abandoned even by their kin. In its virulent form, syphilis was not rampant for more than a few years. Haeser writes: "In the first period of its appearance, the venereal plague often brought the patient to death. Many in the poorest classes—by far the most frequently attacked—died, driven out from among and avoided by their fellow men, even by the lepers, in the streets and fields. But already by 1498 cases of syphilis in which death was an immediate consequence were rare. Cases were much more frequent of sufferings extending over years, often associated with the effects of erroneous treatment. A majority of the deaths seem to have been sudden and due to some particular incident in the course of the disease or its treatment. Thus we read of sudden deaths in a Turkish bath during the salivation, from haemorrhage due to a perforating ulcer of the pharynx, etc." (Haeser, Vol. III, p. 270). By the time of Queen Elizabeth, when an English surgeon, William Clowes, wrote a good clinical account, it is rather the remoter effects and inconveniences than the risk of early death which are emphasized. Here, as in so many aspects of human life, Shakespeare has given a picture of contemporary knowledge which cannot be bettered. It is Timon's address to Phrynia and Timandra:

*"Consumptions sow  
In hollow bones of man! strike their sharp shins,  
And mar men's spurring. Crack the lawyer's voice,  
That he may never more false title plead,  
Nor sound his quilllets shrilly: hoar the flamen,  
That scolds against the quality of flesh,  
And not believes himself: down with the nose,  
Down with it flat: take the bridge quite away  
Of him, that, his particular to foresee,  
Smells from the general weal: make curl'd pate ruffians bald;  
And let the unscarred braggarts of the war  
Derive some pain from you."*

There is no doubt some confusion of our secondary and tertiary classification, but it would be hard to better the summary of what Elizabethan surgeons reported.

It is likely that between the sixteenth and nineteenth centuries the clinical severity of syphilis was still further modified. The great statistician Graunt commented on the rarity of the French pox as a recorded cause of death. He, being a wise man, concluded that only a small proportion of the deaths really due to venereal disease was actually recorded as such, but there is no reason to doubt that had the disease retained anything like its early sixteenth-century virulence in the seventeenth century it would have made a bigger figure in the Bills of Mortality.

Probably only within the last two generations have the laity realized that the great pox, although it does not ravage the world as in the early-sixteenth century, is a serious killing disease. The other important member of the group never had a deadly reputation; such realization as exists that a clap is anything more than a painful experience for the victim and a matter for the jests of his male friends is the fruit of modern education.

Recognition that venereal diseases were in an immense majority of instances contracted only through the sexual intercourse of susceptible with infected persons is nearly as old as the sixteenth-century epidemic. Not quite as old, because so good an observer as Fracastori could not wholly bring himself to believe that the great prevalence was not influenced by miasma. In our time the nature of the *materies morbi* has been completely elucidated.

It might perhaps have been expected that the control of a crowd-sickness the essential nature of which was understood much earlier than that of any other human plague would have been established long ago. No doubt it would have been had real human beings resembled the citizens of Plato's Republic. As they did not, the venereal diseases were as disastrously mismanaged as typhus, and even now there is no very convincing evidence that they are much less of a menace to the communal health than they were at the beginning of the twentieth century. Failure to prevent typhus was—and still is—due to economic incompetence. Failure to prevent venereal diseases was—and still is—due partly to economic and partly to psychological incompetence. Hans Haustein's excellent history of the measures taken to deal with

venereal diseases from the sixteenth to the nineteenth century is an instructive study in human incompetence, and well illustrates the disasters which always befall divided counsels. For reasons which I need not discuss, they are as valid, or—just as the reader pleases—as invalid, in the twentieth as in the sixteenth century, it was a crowd rule that sexual intercourse other than between husband and wife was a sin. Therefore, venereal disease was produced by a sinful action, the victim was a sinner. He or she, however, was also a sick person. Was the victim to be punished for the sin, cured of the sickness, or treated in both ways?

From the beginning a distinction of sex was made; quite soon attempts by the State to punish the male sinner, which had always been a little half-hearted, were generally abandoned. But legislatures were never quite sure in their attitude towards female sick sinners, whether the sin or the sickness was the important consideration. The inevitable result was that their administrative measures failed wholly from both the moral and physical points of view. Sexual sinfulness did not decrease; neither did the incidence of venereal diseases. In most countries the *treatment* of the venereally sick has been pretty completely freed from an associated moral condemnation *on the part of the administrators*. It has not been freed from moral condemnation on the part of an important minority—possibly a majority—of the general public.

The *prophylaxis* of venereal diseases is still in most civilized countries not freed from moral stigma, either administratively or in public opinion.

It is not the business of an epidemiologist to discuss the ethical and psychological reasons for these facts, but it is his business to consider their bearing upon the evolution of venereal diseases as a crowd phenomenon. But these facts themselves make such consideration difficult, because the social taboo, the association of venereal disease with sin, renders the statistical appraisalment of the prevalence either now or in the past wildly conjectural. That consequence was perceived by the father of vital statistics, John Graunt. "We find one *Casualty* in our Bills, of which, though there be daily talk, there is little effect, much like our abhorrence of *Toads* and *Snakes* as most poisonous Creatures, whereas few men dare say upon their own knowledge they ever

found harm by either; and this *Casualty* is the *French Pox*, gotten, for the most part, not so much by the intemperate use of *Venery* (which rather causeth the *Gout*) as of many common Women.

"I say, the *Bills of Mortality* would take off these Bars, which keep some men within bounds, as to these extravagancies: for in the aforementioned 229,250, we find not above 392 to have died of the *Pox*. Now, forasmuch as it is not good to let the World be lulled into a security and belief of Impunity by our *Bills*, which we intend shall not be only as *Deaths heads* to put men in mind of their *Mortality*, but also as *Mercurial Statues* to point out the most dangerous waies that lead us into it and misery; We shall therefore shew, that the *Pox* is not as the *Toads* and *Snakes* aforementioned, but of a quite contrary nature, together with the reason why it appears otherwise.

"Forasmuch as by the ordinary discourse of the World it seems a great part of men have, at one time or other, had some *species* of this Disease, I wondering why so few died of it, especially because I could not take that to be so harmless, whereof so many complained very fiercely; upon inquiry, I found that those who died of it out of the Hospitals (especially that of *Kingsland*, and the *Lock* in *Southwark*) were returned to *Ulcers* and *Sores*. And in brief, I found that all mentioned to dye of the *French Pox* were returned by the *Clerks* of *Saint Giles's* and *Saint Martin's in the Fields* only, in which place I understood that most of the vilest and most miserable Houses of Uncleaness were: from whence I concluded, that only *hated* persons, and such, whose very *Noses* were eaten off, were reported by the *Searchers* to have died of this too frequent *Malady*."\*

The situation now is a little, but not very much, better. Most statisticians are agreed that the actually recorded mortality figures under the heading of, say, syphilis are, even perhaps those of the first year of life, untrustworthy. On the other hand there is some reason to think that the mortality figures are reasonably good *indices* of secular changes.

In the eleven years 1920-30 inclusive, the recorded numbers of deaths from syphilis have been 2,023, 1,799, 1,472, 1,389, 1,296, 1,185, 1,254, 1,406, 1,532, 1,389, 1,414. More than a quarter (in 1930, 27·7 per cent; in 1928, 33·0 per cent) of these deaths are of

\* *Economic Writings of Sir W. Petty*, C. H. Hull, Vol. II, pp. 355-56, 1899.

TABLE 59

STANDARDIZED MORTALITY FROM SYPHILIS IN ENGLAND AND WALES, 1911-28, AT ALL AGES, AND WITH DISTINCTION OF THESE OCCURRING IN CHILDHOOD (0-5) AND IN LATER LIFE

	1911	1912	1913	1914	1915	1916	1917	1918	1919	1920	1921	1922	1923	1924	1925	1926	1927	1928	
Rate per million of all Ages																			
MALES:																			
All ages	..	..	60	63	68	71	62	67	74	72	71	74	64	50	48	42	39	43	50
Under 5	..	..	39	43	47	50	44	47	52	53	54	59	49	35	33	26	24	26	21
Over 5	..	..	21	20	21	21	18	20	22	19	17	15	15	15	15	16	15	17	29
FEMALES:																			
All ages	..	..	45	43	50	52	45	45	52	50	50	56	48	37	30	28	25	26	28
Under 5	..	..	33	31	37	39	33	34	41	39	40	47	38	28	23	20	17	17	15
Over 5	..	..	12	12	13	13	12	11	11	11	10	9	10	9	7	8	8	9	13
Rate of Males per cent of Rate of Females																			
All ages	..	..	133	147	136	137	138	149	142	144	142	132	133	135	160	150	156	165	179
0-5	..	..	118	139	127	128	133	138	127	136	135	126	129	125	143	130	141	153	129
5-	..	..	175	167	162	162	150	182	200	173	170	167	150	167	214	200	188	189	223
Rate at 0-5 per cent of Rate at all Ages																			
Males	..	..	65	68	69	70	71	70	70	74	76	80	77	70	69	62	62	60	49
Females	..	..	73	72	74	75	73	76	79	78	80	84	79	76	77	71	68	65	54

(Taken from Statistical Review of England and Wales, 1928, Table XLVIII, p. 67. Text.)

	1911	1912	1913	1914	1915	1916	1917	1918	1920	1921	1922	1923	1924	1925	1926	1927	1928
<i>Rates per million</i>																	
<b>Males..</b>																	
Syphilis ..	60	63	68	71	62	67	74	72	71	64	50	48	42	39	43	45	50
Tabes dorsalis ..	20	29	32	31	31	34	31	28	27	24	29	26	26	25	26	26	25
G.P.I. ..	95	96	90	94	92	86	96	84	65	61	59	65	55	56	51	54	49
(a) Aneurysm ..	51	51	48	46	45	40	37	33	34	36	35	34	35	34	32	36	37
Total ..	235	239	238	242	230	227	238	217	197	195	180	172	158	154	152	161	161
<b>Females</b>																	
Syphilis ..	45	43	50	52	45	45	52	50	50	56	48	30	28	25	26	29	28
Tabes dorsalis ..	5	6	5	5	5	4	5	4	3	4	5	5	4	5	4	5	4
G.P.I. ..	21	23	20	20	20	17	19	15	12	10	12	13	12	11	11	11	10
(a) Aneurysm ..	11	9	11	10	11	9	10	7	7	7	8	8	7	9	9	9	9
Total ..	82	81	86	87	81	75	86	76	72	77	63	55	51	50	50	54	51

<i>Ratios per cent</i>																	
<b>Males..</b>																	
Syphilis ..	26	27	29	29	27	29	31	33	36	38	35	28	27	25	28	28	31
Tabes do. salis ..	12	12	13	13	13	15	13	13	14	12	14	16	16	16	17	16	16
G.P.I. ..	40	40	38	39	40	38	40	39	33	31	32	36	35	37	34	34	30
(a) Aneurysm ..	22	21	20	19	20	18	16	15	17	19	19	20	20	22	21	22	23
Total ..	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100
<b>Females</b>																	
Syphilis ..	55	53	58	60	55	60	60	66	69	73	66	59	55	50	52	54	55
Tabes dorsalis ..	6	7	6	6	6	5	6	5	4	5	7	8	8	10	8	9	8
G.P.I. ..	26	29	23	23	25	23	22	20	17	13	16	20	22	23	22	22	19
(a) Aneurysm ..	13	11	13	11	14	12	12	9	10	9	11	13	15	18	18	17	18
Total ..	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100

(Op. cit., Table LXIX, p. 72. Text.)

children under five. Details of the changes between 1911 and 1928 are contained in Tables 59 and 60 taken from the Registrar-General's *Statistical Review* of 1928. In the years 1929 and 1930 the rates of mortality were slightly lower than in 1928 (in which year a new form of quasi-confidential death certificate was introduced), viz. 45 and 26 per million living for 1929 and 45 and 25 per million living for 1930. Relatively the adult component of the mortality-rate has greatly increased. Taking the death-rates at ages of 1911 (males) and applying them to the age distribution of the standard million, 60 deaths result, 39 at ages under five, 21 at ages over five. In 1928 the same process allocates 21 deaths to the children and 29 to the adults. This is consistent with a real decline in the mortality at young ages and a slight increase of mortality at adult ages. It is, however, quite probable that the returns with respect to adults are becoming less incomplete, so that the rate of mortality is essentially unchanged. Table 60 brings into account causes of mortality which are known to postulate as a necessary antecedent syphilitic infection. A direct comparison of these statistics is impossible. As we have already seen, the mortality from syphilis itself, so recorded, is largely influenced by mortality in the early years of life; there is no doubt that this has decreased. Mortality from the para-syphilitic diseases presumably reflects the course of syphilitic infection many years before and of treatment some years before. Between 1916 and 1920 mortality from *Tabes dorsalis* decreased from 31 to 24, and has changed little since. G.P.I. has shown a similar but more exaggerated decline within the period 1916-20 and but little movement since. Aneurysm has behaved similarly to *Tabes dorsalis*. There seems no reason to postulate some sudden change of infection-rate at the end of the nineteenth century, and it is easier to believe that improved treatment applied to men under military discipline may have been responsible. So far as these mortality-rates can guide us, they point, in my opinion, to the conclusion drawn in the Registrar-General's *Review* of 1928, viz. that no satisfactory proof that the frequency of syphilitic infection is diminishing is made out.

Unsatisfactory as evidence from mortality figures may be, no better evidence can be found, although a great deal of statistical ingenuity has been devoted to trying to solve the problem,

How many men (or women) will acquire syphilis (or gonorrhoea) before they die?

The earliest candidate for a prize in this guessing competition was F. Lenz, who in 1910 reached the depressing conclusion that more than 100 per cent of the male inhabitants of Berlin acquired syphilis. His method was this. For one place, Copenhagen, he had data for both notifications of syphilis and deaths from G.P.I. For another place (Berlin) he had data of deaths from G.P.I. Using the relation given in Copenhagen and a pseudo-actuarial method, he reached the incredible result just mentioned.

More recent calculators have been more sophisticated. Theoretically the problem is quite simple *if* we know certain facts. Suppose that there were a complete enumeration of attacks of syphilis in a community, and that the resultant attack-rates in age groups had been steady for some years. Suppose, further, that the death-rates from all causes at ages are accurately known. Then we could proceed as follows. We begin, let us say, with 10,000 males aged fifteen; then, having the information postulated, we can calculate the number of these who will acquire syphilis before dying or reaching the age of sixteen, of whom 9,995, say, have not and 5, say, have had syphilis. Proceeding in this way down to the oldest ages until the 10,000 have dwindled to nothing, we shall obtain a column of figures representing the various quotas of new infections at each age. The sum of this column will be the proportion out of 10,000 who have an attack of syphilis before dying. By the use of this method estimates as large as 38·7 per cent for males and 18·5 per cent for females have been reached in respect of Hamburg. For Switzerland the figure is a little more than 3 per cent for males and 1·4 per cent for females. For Sweden as a whole 4·17 per cent for males and 1·73 per cent for females; for Stockholm 17·05 per cent for males, 9·43 per cent for females. The Hamburg data belong to the pre-war period, those for Stockholm to 1915, those for Switzerland to 1920. It is probable that the frequency of syphilis in an urban population is overstated by these calculations, and that of the rural fraction of the total population understated. The attack-rate is usually based upon the ratio of cases reported within the area to the censal population of that area so that if there is an influx of patients to attend city clinics the attack-rate

on the city population will be overstated. Hence we may pretty safely conclude that such a figure as 38 per cent is an overstatement. It is not, however, unduly pessimistic to believe that in the male population of such a country as ours more than 5 per cent and perhaps as many as 10 per cent of males will acquire syphilis before they die. The same method of calculation applied to the statistics of gonorrhoea leads to horrifying results. The Hamburg figure is 155.92 per cent, and even the Swiss figure 12.47 per cent. Naturally here the calculations are even more conjectural, since the same individual may be attacked by gonorrhoea many times, and the data of attack-rates do not distinguish between first and subsequent attacks. Beyond the platitudinous statement that the attack-rate from gonorrhoea is much larger than that from syphilis no cautious statistician would go. It is, however, quite satisfactorily established that the prevalence of the venereal diseases is one of the major facts of epidemiology. Various statistical attempts have been made to relate the incidence of the venereal diseases to economic and social variables. Their success is not great. There is no doubt that the relapse of the European world into acute barbarism from 1914 to 1918 led to an increase of venereal disease only partly set off by better and more energetic anti-venereal therapeutics and prophylaxis. How far variations of post-war practice—still influenced by the ancient confusion of sin and disease—are responsible for the present position nobody can say. Colonel Harrison writes: "In the later years of the war, and for some time after it, propaganda in this country was intense, and it must have had the effect not only of causing the infected to seek treatment early, but also of making them on the whole more careful. In later years propaganda for various reasons was slackened, and I believe that, just as a business declines when it cuts its advertising expenses, so this business of rounding-up the infections in the community became less effective. I have a graph in my own clinic showing a very pronounced decline in its turnover corresponding to a time when advertisements were withdrawn from underground lavatories and a most pronounced rise corresponding very closely to the week when the advertisements were replaced."\* The temptation to enlarge upon that quotation is great, but I am able to resist it. I do not doubt in the least that

\* *Proc. Roy. Soc. Med.*, Vol. XXIV, 1931, p. 1093.

if the psychological attitude of the crowd towards the performance of the sexual act were similar to its attitude towards eating and drinking, playing golf, or driving an automobile, venereal diseases would cease to have any real epidemiological importance. But the little fact that in writing the last sentence I have substituted a silly periphrasis for the colloquial equivalent of the colloquial words eating and drinking, and the big fact that complete failure to deal intelligently with the less psychologically complex crowd issues of buying and selling has already brought civilization to the brink of destruction, are enough to prove that the moralizing of a professor of epidemiology upon the subject would be impertinent in every sense of the word.

There is, I think, this ground for optimism. That on the whole the crowd attitude, as expressed in its administrative rules and its social reactions, is a little saner than before the war. But this generation will have passed away, and many billions of words will have been spoken before the most eminently preventable of all crowd-sicknesses are actually prevented.

#### RECOMMENDATIONS FOR FURTHER STUDY

Haustein's article in the third volume of the *Handbuch der sozialen Hygiene und Gesundheitsfürsorge*, edited by Gottstein, Schlossmann, and Teleky (Berlin, 1925), is, I think, a satisfactory account of the modern history of the subject. The best introduction to the older history is Haeser's account in the third volume of his *Lehrbuch der Geschichte der Medizin*.

## XIV

### TUBERCULOSIS

TUBERCULOSIS, like the venereal diseases, does not normally behave like what the man in the street would call an epidemic disease, i.e. its incidence in time does not vary abruptly.

Under some circumstances, for instance when uncivilized races are brought into intimate contact with the white races, or when particular populations are subjected to very abnormal conditions of life, tuberculosis may behave in this way. It is not a very artificial use of language to say that in the last years of the war tuberculosis was seriously epidemic in the mental hospitals of England and Wales. Table 61 shows how the mortality rose to almost four times its normal rate and how rapidly it again declined.

There is no doubt as to how this "epidemic" was generated; it was an unintentional illustration of the fact that a principal determinant of mortality from tuberculosis is nutrition. The mortality statistics of the whole population of Prussia gave a larger-scale demonstration of the same law (see Table 62).

If one examines the mortality statistics of a settled country over the last eighty years one indeed finds a change, a decrease of mortality. Since 1851-5 to 1926-30 the standardized rate of mortality from all forms of tuberculosis (persons) in England and Wales has declined from 3,638 per 1,000,000 to 922 per 1,000,000 and although the quinquennial rate of decline has not been constant the actual decline has never been interrupted by an increase. Seasonal mortality, again, is not constant. In 1930 there were as few as 1,295 deaths of males in one month (August) and as many as 1,987 in another (March), but that is but a small movement in comparison with the swing of such a typical "epidemic" disease as measles, the monthly deaths of males from which varied from 33 in September to 522 in March. As an object of normal epidemiological study we must look upon tuberculosis as a very old crowd-sickness, one which has been a principal factor of mortality for more than two thousand years, a fact which gives us certain advantages and imposes some disadvantages. While our knowledge of individual "cases" of, say, measles or typhoid

# TUBERCULOSIS

343

TABLE 61  
MENTAL HOSPITALS. MORTALITY (PRIMARY AND SECONDARY) FROM DYSENTERY AND TUBERCULOSIS

Year	Daily Average Number of Patients Resident	Dysentery		Tuberculosis						Dysentery	Tuber- culosis (all forms)
		Number of Deaths	Mortality per 1,000 Resident	Phthisis		Other Forms		Total		Mean of Group	Mean of Group
				Number of Deaths	Mortality per 1,000 Resident	Number of Deaths	Mortality per 1,000 Resident	Number of Deaths	Mortality per 1,000 Resident		
1910	98,505	251	2.5	1,355	13.8	189	1.9	1,544	15.7	2.8	16.5
1911	100,552	301	3.0	1,333	13.3	207	2.1	1,540	15.3		
1912	102,647	287	2.8	1,398	13.6	342	3.3	1,740	17.0	7.7	13.7
1913	104,868	270	2.6	1,471	14.0	376	3.6	1,847	17.6		
1914	106,451	345	3.2	1,476	13.9	330	3.1	1,806	17.0	1.7	11.2
1915	102,724	595	5.8	11,793	117.5	1,220	12.1	12,013	119.6		
1916	101,539	648	6.4	12,000	119.6	1,250	12.5	12,250	122.1	131.9	13.7
1917	98,621	1,143	11.6	13,168	132.1	1,496	15.0	13,664	137.2		
1918	90,459	928	10.3	14,128	145.6	1,557	16.2	14,685	151.8	1.7	11.2
1919	87,215	394	4.5	12,399	127.5	1,337	13.9	12,736	131.4		
1920	90,950	212	2.3	1,251	13.8	361	4.0	1,612	17.7	1.7	11.2
1921	94,320	238	2.5	1,244	13.2	253	2.7	1,497	15.9		
1922	98,314	177	1.8	1,155	11.7	222	2.3	1,377	14.0	1.7	11.2
1923	102,076	116	1.1	870	8.5	193	1.9	1,063	10.4		
1924	104,137	104	1.0	941	9.0	223	2.1	1,164	11.2		

fever is the product of observation through only a few hundred years, our clinical knowledge of tuberculosis goes back two thousand years. The Greek, Graeco-Roman, and Arabian physicians did not know as much of the pathological and biological details of the process as we do; they lacked various methods of diagnosis and treatment available to us. But their knowledge was congruent with ours. If Galen were to come among us from the

TABLE 62

ANNUAL RATE OF MORTALITY FROM TUBERCULOSIS PER 10,000  
POPULATION IN PRUSSIA, 1900-29

Year	Rate	Year	Rate
1900	21.1	1915	14.6
1901	19.5	1916	15.8
1902	19.0	1917	20.5
1903	19.7	1918	23.0
1904	19.2	1919	21.9
1905	19.1	1920	15.8
1906	17.3	1921	13.5
1907	17.2	1922	14.3
1908	16.5	1923	15.3
1909	15.6	1924	12.2
1910	15.3	1925	10.9
1911	15.1	1926	10.0
1912	14.6	1927	9.6
1913	13.7	1928	8.9
1914	13.9	1929	8.9

world of "discarnate intelligence"—wherever that is and whatever it may mean—and to read a modern textbook on medicine, some passages in the article on tuberculosis would puzzle him, but he would get the hang of the whole and a good deal of the treatment would be quite familiar to him. The article on typhoid fever would be almost wholly unintelligible to him; most of the concepts and much of the recorded clinical experience would be quite unfamiliar. Much current discussion on tuberculosis, for instance that on the relative importance of seed and soil, is only a continuation of a controversy more than a thousand years old, and it was the elder Pliny—who died in A.D. 79 and copied *his* prescription from somebody else—who taught that residence in

the open country, particularly in pine-wood country, was more profitable to phthisics than even drinking milk on the mountains in the summer. Therefore we have the advantage of a long experience; the subject has been meditated on by men who knew what they were talking about for a very long time. On the other hand, this duration imposes some disadvantages. Of scarlet fever, of plague, and perhaps of smallpox, we in Western Europe have seen the beginning and the end or, if not the end, at least a profound modification of type. Plague has gone, typhus has gone, scarlet fever and smallpox are (in Western Europe and in our generation) mere shadows of their former mighty selves. Tuberculosis is faltering; its striking power is not much more than a quarter of what it was in the days of our grandparents, but it will be some little time before this giant whose conquest has so often been proclaimed cuts short fewer than thirty thousand lives of English people in a year. The facts that tuberculosis is still so deadly and yet has decreased so much within three generations pose a question which is hard to answer. Even now our statistical information is not precise; before 1838 it was hopelessly vague. What was happening to tuberculosis before the statistical record began? Was there any period when the rate of mortality was *less* than ninety years ago? Was the decrement which began in the 'fifties of the last century the first improvement, or has tuberculosis, like scarlet fever, had ups and downs before our day?

At the beginning of the nineteenth century a quite interesting discussion of this point was begun by Dr. William Woolcombe of Plymouth, whose remarks on *The Frequency and Fatality of Different Diseases, Particularly on the Progressive Increase of Consumption*, appeared in 1808. Woolcombe proceeded in the following way. He abstracted the London Bills of Mortality from 1650 to 1800, and observed that the ratio of deaths from consumption to deaths from all causes which had been 1 in 5 in the first half of the eighteenth century was 1 in 3 in the last ten years of it. He then instanced the mortuary records of the parish of Holycross, near Shrewsbury, which had been collated by Haygarth and published in the *Philosophical Transactions*. Here the registers were thought to have been very well kept and the population to have been stationary. No strangers had happened to die in the parish during the period of observation, nor were

names of non-parishioners buried in the churchyard inserted in the register. The names of parishioners who died elsewhere were, however, entered. In the ten years from 1750 the whole mortality was 290; of these 47 deaths assigned to consumption. From 1760 to 1770 the total of burials was 365, 101 from consumption. The ratio has changed from 1 in 6 to 1 in 3.6. From 1770 to 1780 the proportion of mortality from consumption is said to have been 1 in 5. Other records are given showing high proportions; for instance, for Warrington in the year 1773 there were 96 instances of consumption in 288 burials, 1 in 3. As Woolcombe did not know what the actual death-rates were he had to use a sort of *ex absurdo* argument. If the death-rate at the beginning of the century had been 1 in 36, and if the death-rate from consumption had remained constant but the proportion of deaths from consumption among all deaths had increased by one-third down to the beginning of the nineteenth century, then it would follow that the general death-rate must have fallen to 1 in 54; that, however, must be wrong, because the very incomplete population registers of the last six years of the eighteenth century when related to the census enumeration produced a mortality figure of 1 in 47. Reversing the process, i.e. assuming that the rate of mortality for 1801 was known, and deducing the rate for the beginning of the eighteenth century, he found that if the rate of mortality in 1800 were 1 in 40 it must have been 1 in 27 in 1700 unless the rate of mortality from phthisis had changed, and a mortality-rate of 1 in 27 in 1700 he thought implied "a degree of unhealthiness inconsistent with the known conditions of the country at that period." The principle is a sound one, but Woolcombe had, I think, overlooked the fact that his most important data related to London, and it is by no means inconsistent with the known conditions to suppose that in *London* the rate of mortality at the beginning of the eighteenth century may have been nearer 1 in 20 than 1 in 30. Woolcombe—who, it may be interjected, was much more circumspect than many of his successors in the handling of that chancey instrument proportional mortality—also noted the difficulty that his calculations depended on the assumption of a constant age composition of the exposed to risk, and recognized that the high proportional mortality from phthisis in London might be due to migration of

young lives. "This circumstance," he writes, "may perhaps account for the greater proportion of phthisical mortality in London compared with the country and other towns of less magnitude, but cannot be allowed to have any influence on the relations subsisting in London at different periods, because the metropolis must at all times have drawn its recruits from the country under similar circumstances" (op. cit., p. 59). This latter contention does not seem unassailable, because the importance of the out-parishes increased throughout the eighteenth century, and their age and sex constitution may have changed greatly as the commercial character of London changed. Woolcombe does not inquire whether the attribution of deaths to the heading consumption may not have changed, but there seems no good reason to suppose that it did. I think the most serious weaknesses in his case are the impossibility of making due allowance for the age constitution of the exposed to risk and the undue weight given to London experience. The great Farr tackled the problem in his first important paper, published in McCulloch's Statistical Account of the British Empire. He dealt not with the whole of London, but only with London within the Liberties, the population of which had actually been enumerated in 1631 and printed by Graunt; it amounted to 130,178, which was almost identical with the enumerated total (corrected for non-residents) of 1821, 130,100. Taking the population to be stationary (i.e. not merely constant in numbers but in age and sex composition) he reached these results. Between 1629 and 1635 he made the general death-rate 50 and that from consumption 10 per 1,000. From 1660-79, 80 and 13 per 1,000; from 1728-57, 52 and 9 per 1,000; from 1771-80, 50 and 11 per 1,000; from 1801-10, 29 and 7 per 1,000; and from 1831-5, 32 and 6 per 1,000. He concluded that the *relative* importance of consumption increased down to 1810, but that, excepting in the anomalous period of 1771-80, the actual death-rate had always declined. Farr also probably contributed the statistics of Sir James Clark's book on phthisis, published in 1835. These figures purported to give the rate of mortality from phthisis of the whole population of London within the Bills of Mortality. There was an increase from 4 per 1,000 in 1700 to 6.6 in 1750, and thereafter fluctuation around 6 until 1821, the last date entered. Sir Gilbert Blane writing in

TABLE 63  
COMPARATIVE DEATH-RATES FROM PHTHISIS AT AGES—MALE AND FEMALE

	10-15		15-20		20-25		25-35		35-45		45-55		55-65		65-75		75 and over	
	M.	F.	M.	F.	M.	F.	M.	F.	M.	F.	M.	F.	M.	F.	M.	F.	M.	F.
<i>England and Wales</i>																		
1851-60	100	169	100	147	100	106	100	114	100	105	100	82	100	72	100	69	100	77
1861-70	80	137	92	130	96	98	102	109	104	97	101	75	99	62	85	52	72	48
1871-80	63	111	70	100	77	78	92	88	103	85	101	64	96	53	81	46	65	44
1881-90	45	92	54	75	58	57	75	70	89	68	91	54	87	45	76	41	75	43
1891-1900	31	66	41	54	47	39	59	48	77	53	82	43	78	37	66	34	60	38
1901-10	22	52	32	41	38	30	49	37	61	39	72	34	71	31	64	32	61	39
<i>London</i>																		
1881-90	38	70	49	50	56	40	94	64	132	81	143	67	139	54	113	44	123	57
1891-1900	26	54	40	40	48	29	75	46	119	68	133	59	130	47	115	43	119	59
1901-10	20	43	33	33	40	24	58	33	91	47	114	47	115	42	114	43	122	64
<i>Bedfordshire</i>																		
1881-90	32	104	29	75	50	59	65	73	69	64	69	54	52	45	75	40	26	52
1891-1900	17	44	31	43	39	37	57	49	61	38	60	44	53	41	44	31	39	43
1901-10	23	49	30	37	40	32	46	32	47	34	50	24	46	36	32	27	21	35
<i>Lancashire</i>																		
1881-90	55	94	64	78	61	61	81	78	103	78	106	61	97	52	78	43	81	56
1891-1900	38	69	45	55	46	41	62	53	95	63	101	48	87	39	77	35	55	36
1901-10	28	58	35	43	36	31	51	40	76	45	95	41	92	36	75	34	73	48
<i>Sussex</i>																		
1881-90	36	73	44	67	58	51	85	62	94	65	93	53	89	45	70	34	86	19
1891-1900	23	59	39	50	51	38	65	43	79	46	79	42	77	35	61	37	56	37
1901-10	17	47	28	38	47	26	61	31	64	33	66	28	66	28	59	35	74	37

(Taken from "Epidemiology of Pulmonary Tuberculosis," by M. Greenwood, *Annual Report of the C.M.O., 1919-20*, p. 327.)

1815 made the singular and perhaps prophetic remark that "consumptions have been observed to be more frequent of late among young adults, probably from a greater number of sickly children being saved." He thought that infant mortality was falling.

These points of view are interesting, and we may at least infer that no great changes of mortality from phthisis occurred between the end of the Stuart period and the beginning of the nineteenth century—certainly no improvement. Nor was there much change in the first twenty years of the Victorian epoch. But around the early 'fifties of the nineteenth century a change began (see Table 63).

This decline began earliest in the younger age groups. Already in 1861-70 the rate of mortality upon children at the end of school life had fallen 20 per cent, a decline of similar magnitude had been experienced by young adults ten years later, in 1871-80; in 1881-90 the wave had reached those aged 25-35; by 1891-1900 men of 35-45 had only 77 per cent of the mortality of 1851-60; and by 1901-10 those past the prime of life were similarly affected (see Table 64). If one makes a mere crude comparison of national rates it will be seen that, with few exceptions, other West European States have participated in the movement (see Table 65).

The world war temporarily interrupted this progress, but only temporarily; some epidemiologically interesting changes have indeed been observed—notably the stasis of mortality-rates on young women, which has been a widely observed feature of post-war experience—but, broadly speaking, here and elsewhere the setback due to the war has been recovered from and mortality-rates are as low as or even lower than they would have been had the rate of progress observed immediately before the war continued without interruption.

This change has been so great—thus, in the year of maximum recorded mortality, 1850, the standardized rate per million persons for tuberculosis of the respiratory system was 1,748, in 1928 it was 709—that naturally many explanations have been proposed. Most of them contain some truth; none of them can possibly be the whole truth. My business is not to detail all or even the most plausible of these hypotheses, but to try to give some indications of where, in my judgment—which is, of course, just as fallible as that of all other men—most truth lies. There are three main tendencies in hypothesis-making; each is motivated

TABLE 64

THE UPLINE OF PHTHISIS AS OBSERVED AND AS WOULD HAVE BEEN OBSERVED HAD THE REDUCTION FOLLOWED  
A GEOMETRIC RATE OF DECREASE

(At ages 10-35 the common ratio 0.791, and at ages 35 and over the common ratio 0.837, has been used)

	10-15		15-20		20-25		25-35	
	Males	Females	Males	Females	Males	Females	Males	Females
1851-60	100	169	—	147	—	—	—	—
1861-70	80 (79)	137 (134)	92	130 (116)	96	98	—	109
1871-80	63 (63)	111 (106)	70 (73)	100 (92)	77 (76)	78 (78)	92	88 (86)
1881-90	45 (49)	92 (84)	54 (58)	75 (73)	58 (60)	57 (61)	75 (73)	70 (68)
1891-1900	31 (39)	66 (66)	41 (46)	54 (58)	47 (47)	39 (48)	59 (58)	48 (54)
1901-10	22 (31)	52 (52)	32 (36)	41 (46)	38 (38)	30 (38)	49 (46)	37 (43)

	35-45		45-55		55-65	
	Males	Females	Males	Females	Males	Females
1851-60	—	—	—	82	—	72
1861-70	—	97	—	75 (69)	—	62 (60)
1871-80	103	85 (81)	101	63 (57)	96	53 (59)
1881-90	89 (86)	68 (68)	91 (85)	54 (48)	87 (80)	45 (42)
1891-1900	77 (72)	53 (57)	82 (71)	43 (40)	78 (67)	37 (35)
1901-10	61 (60)	39 (48)	72 (59)	34 (34)	71 (56)	31 (30)

(M. Greenwood, op. cit., p. 329.)

by the perception of certain unchallengeable scientific facts and each congruent with the mental make-up of different types of human personality.

First we have the medical tendency. The history of medical research into the aetiology of tuberculosis during the nineteenth century is one of the most brilliant chapters in the story of the profession; beginning with the work of Laennec, continued by Gendrin, Lobstein, Andral, Louis, Schönlein, and Rokitansky, the pathological anatomy of the disease was thoroughly elucidated; then in the 'sixties of the century Villemin proved directly what before had been only inferential, that tubercle was a specific infective disease communicable by an inoculum; finally, almost fifty years ago, Koch, by the isolation of the actual virus of tuberculosis and the demonstration of the unity of tubercle as a pathological process, placed the corner-stone on the edifice. It would have been strange indeed if tough-minded, enthusiastic persons, practical men—to whom we owe most of the conveniences and all the horrors of modern life—had not believed that these great discoveries placed in their hands a whole arsenal of means for eradicating tuberculosis. It must have seemed to them that tuberculosis was much more at their mercy than, say, scarlet fever and measles. True, these were infectious diseases, to be met by shutting up infective persons and disinfecting their dwellings. But they were acute diseases which might, and did, spring into epidemic activity unawares, leading to hundreds of cases within a short space of time. Phthisis, on the other hand, was a slow process and again, unlike measles or scarlet fever, its germ was visible and could be made the subject of deliberately directed attack. To these considerations we owe not only the methods of attack devised, but also the attempted demonstrations that these methods were in fact responsible for the success attained. This philosophy of tuberculosis always has appealed and always will appeal to tough-minded people, who, unconsciously, take a sacerdotal view of the status of the medical profession, who delight in giving orders and instruction to the laity.

Next in importance is what I may call the humanitarian school, which combines tough- and tender-minded people in an unknown proportion. Statistically speaking—of course there are numerous exceptions—its psychological motive is a distrust or dislike of

TABLE 65

MORTALITY FROM TUBERCULOSIS IN EUROPE PER 10,000 POPULATION FROM 1871 TO 1923

Countries placed in Order of Death-rate, 1906-10	1871-7	1876-80	1881-5	1886-90	1891-5	1896-1900	1901-5	1906-10	1911-14	1920-3
Belgium .. ..	33.58	32.31	30.11	—	28.84	24.88	—	12.88	13.50§	—
England and Wales ..	29.41	28.91	25.42	23.23	21.19	19.04	17.44	15.68	13.89	11.11
Russia .. ..	—	31.72	31.29	29.04	24.72	20.79	19.14	16.21	14.32	14.64
Denmark* .. ..	—	31.31	30.49	28.93	26.85	21.61	19.29	16.24	14.60	—
Netherlands .. ..	—	—	—	—	—	—	18.66	16.56	14.55	12.15
Italy .. ..	—	—	—	20.83	19.19	18.08	16.65	16.73	15.38	13.87
Germany .. ..	—	—	—	—	—	—	20.66	17.53	14.96	14.61
Scotland .. ..	35.63	33.61	29.70	25.83	24.10	23.36	21.60	20.21	17.00	11.96
France (total) .. ..	—	—	—	—	—	—	—	22.13	21.93§	—
Norway .. ..	—	—	—	—	—	26.87	25.57	24.00	—	20.24
Switzerland .. ..	—	—	27.08	27.02	25.36	24.62	26.52	24.68	20.24	16.28
Ireland .. ..	25.29	26.62	26.59	26.92	27.49	28.25	27.57	25.26	21.41	—
Finland† .. ..	41.40	36.68	25.52	25.58	—	27.25	29.08	27.21	26.00	20.80
Austria .. ..	—	37.73	39.33	38.30	39.39	33.95	34.07	30.53	22.80	23.04
France† .. ..	—	—	—	—	33.60	32.36	32.17	32.23	—	—
Hungary .. ..	—	—	—	—	—	32.77	39.63	37.44	33.42	29.89

\* Large towns.

† Only phthisis.

‡ Towns over 5,000 population.

§ 1911-13.

|| 1920-2.

(Taken from "Einige methodologisch-statistische Studien zur Epidemiologie der Tuberkulose," Greenwood and Wolff,  
*Zeitschrift für Tuberkulose*, 1928, Band 52, p. 99.)

professional science. In the days of our grandparents Chadwick was a typical example of this group. He had all the zeal for practical measures of the first group, but he never knew or cared anything for laboratory or mathematical science. A much more complex character, Florence Nightingale, was of the same kind. In our day the type flourishes among strong-minded philanthropists and self-sufficient borough councillors, who do not hold with medical nonsense, but are firm believers in good housing and proper feeding of the working classes. It also includes all those tender-minded people whom we contemptuously term faddists—as some of them, of course, are—and sentimentalists.

The slogan of this group is that none of the medical nostrums have been of the least importance, that the way to get rid of tuberculosis is not to fuss about bacilli and such nonsense, but to feed, clothe, and house people better.

Lastly, we have the biological group; these are differentiated from and regard both the former groups with a pretty impartial contempt. The altar of their idolatry is pure science; they despise the medical group because medical science is so slap-dash—people going about the world talking of science who could not integrate the simplest differential equation nor tell the difference between a homozygote and a heterozygote; they loathe the second group, members of which do not believe in science of any kind.

Members of each of these groups have published analyses of the causes of decline of tuberculosis during the last seventy-five years. Thus from the first group we have had attempts to demonstrate statistically that tuberculosis mortality has declined in linear fashion since the beginning of the modern epoch; if, it said, the decline has been linear, then, since this means that the percentage decrease—the constant decrement being related to the diminishing ordinate—is increasing, we may infer that the main factor of decline has been the increasing utilization of medical methods—improved facilities for segregation, wider use of such measures as tuberculosis dispensaries.

The second group has rejoined that the declining curve may as plausibly be related to the rising curve of real wages, and insists upon the spatial as well as chronological relationship between increase of well-being, in a general sense, and decrease of tuberculosis. For instance, while it is a fact that in a homo-

geneous country within which the standard of living is uniformly high tuberculosis is more fatal in industrial than in country districts, it is not a fact that, taken in the large, agricultural countries have less mortality from tuberculosis than industrial States; in Germany, for instance, the rate of mortality from tuberculosis is higher in the relatively agrarian State of Bavaria than in the intensely industrialized State of Saxony.

The third group has pointed out that, in England and Wales, the course of mortality from tuberculosis in time is certainly not adequately represented over the whole period by a single straight line, and has suggested that the experience may be more satisfactorily represented by breaking it up into three, of which the second, which described the period from about 1865 to 1890, had a much steeper inclination to the base line than the third. The inference drawn was that in the days of our most active efforts in the public health field, mortality from tuberculosis was declining more slowly than before. Professor Karl Pearson, indeed, writing at the end of the war, said: "On the whole, it is risky to form a very definite judgment, but having regard to the female phthisis death-rate and to the percentage of the phthisis death-rate on the general death-rate, war difficulties do not seem to me sufficient to obscure the general trend of our graphs (as indicated before the war); namely, that somewhere about 1915 the fall in the phthisis rate which had been less rapid since 1895 would cease altogether, and probably be followed by a *rise*. The next five years will show whether this be true or not. We should expect a fall in the phthisis death-rate immediately, but on the average the value will remain higher than that of 1915."

So far as the statistical proofs of the first class are concerned, critics of the third group have had an easy enough task. It is easy to demonstrate that so simple a locus as a straight line does not satisfactorily represent the trend of mortality, and that such a locus used for extrapolatory purposes will lead to ridiculous results. It has also been easy to ridicule the surprising conclusions which misinterpretation of the method of correlation may lead to, when, tacitly substituting the notion of causation for that of correlation, one attempts to demonstrate, for instance, that a principal factor of the decline of mortality from pulmonary tuberculosis has been the segregation of "open" cases. But, on

the other hand, it may be urged that not only is the subdivision of the epoch into three ostensibly linear trends very arbitrary, but that, tried by the test to which he appealed, Professor Pearson's own rather gloomy prophecy has not been fulfilled.

Avoiding the falsehood of extremes which each of these parties has exemplified, we may no doubt achieve no more valuable a result than the summing up of Mr. Justice Stareleigh in the action of *Bardell v. Pickwick*. It is so very easy to say that there is some truth in the contentions of all parties, and the saying

TABLE 66  
RATES PER 100,000 FROM ALL FORMS OF TUBERCULOSIS

District	1886-8		1903-5		1913		1926	
	Town	Country	Town	Country	Town	Country	Town	Country
Hannover ..	338	329	203	222	135	145	86	115
Hildesheim ..	239	263	230	194	148	115	118	75
Lüneburg ..	275	283	211	155	167	78	98	65
Stade ..	305	361	138	210	111	103	125	75
Osnabrück ..	440	451	230	283	177	138	128	95
Aurich ..	259	306	171	232	140	123	147	114
Minden ..	378	415	198	232	150	120	128	95

(Taken from Prinzing's *Handbuch der Med. Statistik*, p. 575, 1931.)

of it does not guarantee superior wisdom or impartiality; it may only be a mark of mental inertia.

Before attempting to sum up, even in the manner of Mr. Justice Stareleigh, a little more evidence needs consideration. The modern experience of England and Wales that mortality from tuberculosis is higher in urban than in country districts is not by any means a universal experience. Table 66 relating to some administrative districts of Prussia shows that even as recently as 1926 country mortality from tuberculosis was greater than town mortality in one area.

Here the overcrowding of sleeping-rooms in the country has been held answerable. Again, in relatively unurbanized countries like Hungary mortality from tuberculosis is far higher than in such highly industrialized areas as Saxony or England and Wales. Here, again, attention has been directed to the fact that where

TABLE 67

LONDON BOROUGHS

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District	Domestic Servants (Both Sexes Per Cent of Population, 1911)	Death-rate from all Causes, 1911-13		Infant Mortality			Death-rate from Tuberculosis, 1911-13	
		Crude	Standardized	1918-19		Total	Crude	Standardized
				Legitimate	Illegitimate			
Kensington .. ..	16.67	13.7	13.6	83	221	112	1.32	1.32
Hampstead .. ..	16.40	10.4	11.0	64	236	72	0.81	0.80
Westminster .. ..	15.17	12.6	13.3	77	235	94	1.49	1.42
Chelsea .. ..	14.96	14.7	14.0	78	155	91	1.64	1.61
Marylebone .. ..	12.98	14.3	14.6	79	250	98	1.70	1.66
Paddington .. ..	10.42	13.3	13.2	88	237	109	1.33	1.31
Group I .. ..	14.38	13.2	13.4	80	228	100	1.39	1.36
City .. ..	6.46	14.0	14.6	122	278	97	1.95	1.84
Lewisham .. ..	5.71	11.3	11.1	51	294	84	1.09	1.01
Wandsworth .. ..	5.67	11.5	11.6	72	240	96	1.20	1.18
Stoke Newington .. ..	4.98	13.0	12.4	71	231	85	1.30	1.28
Holborn .. ..	4.38	15.1	15.2	99	267	102	2.30	2.17
Greenwich .. ..	4.10	13.9	13.7	93	349	102	1.60	1.59
Group II .. ..	5.34	12.2	12.1	73	272	94	1.32	1.30

## TUBERCULOSIS

357

Fulham	..	..	3.52	13.6	14.1	85	222	105	1.73	1.69
Hammersmith	..	..	3.30	14.5	14.3	91	207	114	1.62	1.58
Lambeth	..	..	3.18	14.3	14.0	82	217	105	1.71	1.68
St. Pancras	..	..	3.12	15.1	15.1	81	226	98	1.91	1.85
Hackney	..	..	2.95	13.5	13.6	83	355	100	1.68	1.67
Woolwich	..	..	2.81	12.6	12.9	88	220	84	1.67	1.65
Camberwell	..	..	2.68	13.8	13.6	83	268	99	1.61	1.60
Deptford	..	..	2.64	15.0	14.8	87	176	117	1.73	1.70
Battersea	..	..	2.62	13.6	13.7	74	276	107	1.56	1.53
Islington	..	..	2.48	14.9	14.5	88	258	107	1.69	1.66
Group III	..	..	2.90	14.1	14.0	84	243	103	1.70	1.67
Stepney	..	..	1.33	15.8	16.5	90	314	121	2.15	2.12
Finsbury	..	..	1.24	18.6	18.4	91	229	137	2.47	2.45
Southwark	..	..	1.23	17.5	17.6	101	225	122	2.23	2.17
Poplar	..	..	1.18	17.2	17.0	92	216	125	1.88	1.86
Bermondsey	..	..	0.97	17.8	17.8	105	360	133	2.35	2.31
Shoreditch	..	..	0.91	18.9	19.5	124	255	150	2.47	2.46
Bethnal Green	..	..	0.77	16.4	17.1	101	263	123	2.21	2.21
Group IV	..	..	1.13	17.1	17.4	99	260	128	2.21	2.18
County of London	..	..	4.74	14.4	14.4	86	247	109	1.71	1.68

(Taken from "The Incidence of Mortality upon the Rich and Poor," by T. H. C. Stevenson, *Jl. Roy. Stat. Soc.*, Vol. LXXXIV, 1921, p. 91.)

tuberculosis ravaged country districts the economic standard of life was very low, and the coming of industry brought more relief to economic pressure than, possibly, increased opportunities of infection neutralized.

Returning to the conditions of our own country, the following points are to be noted.

Mortality from tuberculosis increases considerably as one passes from the economically prosperous to the poor districts of any area. Table 67 from Dr. T. H. C. Stevenson's paper illustrates the relation.

Passing from the most to the least prosperous group, although

TABLE 68

Tin and copper miners	..	..	..	..	8,394
Metal-grinders	..	..	..	..	4,117
Slate masons and slate-workers	..	..	..	..	3,341
Potters' mill workers, slip-makers, potters	..	..	..	..	2,625
Barmen	..	..	..	..	2,613
File-cutters	..	..	..	..	2,407
Drafters and brush-makers	..	..	..	..	2,314
Costermongers, hawkers, and street sellers	..	..	..	..	2,234
Earthenware, china, etc., kiln and oven men	..	..	..	..	2,167
Brass foundry, furnacemen, and labourers	..	..	..	..	2,118
Stevedores	..	..	..	..	2,113
Cutlers	..	..	..	..	2,075
Masons, stone-cutters, and dressers	..	..	..	..	2,050
Metal glazers, polishers, buffers, and moppers	..	..	..	..	2,024

general mortality (standardized) increases no more than 29.9 per cent, mortality from tuberculosis increases by more than 60 per cent. This relation, striking as it is, falls far short of that observed in Paris by Hersch, who was able to express the mortality from tuberculosis in the various administrative divisions of Paris almost as a mathematical function of a measure of poverty. Still, even the English data suffice to bring out the essential potency of this economic factor, to show how just was the characterization of phthisis as a *morbus pauperum*. It is not scientific or modern-minded or anything but foolish to try to believe that any other prophylaxis of this particular crowd-disease is so important as raising the economic level and increasing the *commoda vitae* of the crowd.

It would, however, be false to say that poverty is the only

aetiological factor we need consider. Table 68 based on the most recent evaluation of mortality in occupations (1921-3) contains the fourteen groups with mortality from all forms of tuberculosis more than twice that of all occupied and retired males (taken as 1,000).

This list includes only one occupation, that of street hawkers, where the aetiological factor of poverty can unhesitatingly be regarded as primary, and at least nine wherein a special occupational hazard, viz. exposure to the action of siliceous particles, is known to prevail. Again, when we compare the mortality from tubercular diseases through the whole list of occupations, we discover groups or sub-groups whose mortality from tuberculosis, although far short of qualifying them for inclusion in the list of terrible examples, is greater than can be explained on economic grounds. A notorious example is the printing industry. Hand compositors and machine compositors have general mortality figures practically normal, 1,007, and appreciably below normal, 867; their comparative mortality figures from tuberculosis are in each instance much above normal, 1,288 and 1,252. The infant mortality figures for these groups (excellent social indices) are low, and, of course, they belong to the upper stratum of the wage-earning classes. Special efforts have been made to explain such cases, but with only partial success. The most complete study of the sickness and mortality experience of the printing industry, that of Dr. A. Bradford Hill, leads to the general inferences that: (1) the recruitment by the industry of persons of poor physique—since great manual strength is not an essential requirement; (2) unfavourable working conditions (for instance, opportunities for droplet infection, in small and crowded composing rooms) are principal factors. Essentially similar conclusions have followed investigation of tuberculosis in the boot and shoe industry.

One may perhaps sum up in this way. The genesis of active tubercular disease involves three factors: (1) a seed; (2) a soil; (3) some methods of husbandry. Of these three, only the first is essential. Given a sufficiency of seed, the plant will grow in any soil and without any gardener's attention. In actual life, variations of the two non-essential factors are of great importance. It may well be that increasing numbers of people survive who

some generations ago would have perished under the environmental hardships of their time, and that the population now contains a larger proportion of those constitutionally prone to succumb to the infection of tuberculosis when the dosage is less than would have been needed to destroy their forebears. But it is probable that changes of husbandry, and eliminations of the specific fertilizers, such as siliceous dust, and supply of the numerous general fertilizers which encourage fruit and flowers but discourage weeds, keep pace with, indeed outstrip, the other change.

At the worst, looking at the position epidemiologically, we might fear that if a population such as ours were, through the breakdown of the machinery of civilization, again exposed to the environmental conditions of a city slum of the eighteenth- or early nineteenth-century type, the reaction in terms of tuberculosis would be sharper than in the past.

Without doubt, it is idle to speak of the conquest of tuberculosis; tuberculosis has not been and so far as one can see never will be conquered. We may, however, reasonably expect a further decline of mortality, provided that our means allow us to improve the general environmental conditions of the people.

#### RECOMMENDATIONS FOR FURTHER STUDY

The literature is so immense that recommendations are futile. I can only mention one or two books which the reader might but should not miss.

Bushnell, G. E. *A Study of the Epidemiology of Tuberculosis.*

Brownlee, J. *An Investigation into the Epidemiology of Phthisis in Great Britain and Ireland*, Medical Research Council, Special Report Series, Nos. 18 and 46.

## XV

### CANCER

OUR consideration of the epidemiology of tuberculosis carried us some way from the conventional field of old textbook epidemiology, but there was at least a thread of connection inasmuch as tuberculosis is known to be an infectious disease. When we approach the study of cancer that thread snaps, because, using the word "infectious" in any ordinary sense, there is no reason whatever to think that cancer is infectious.

From the statistical point of view there is no doubt that cancer is one of the most important crowd-sicknesses, and, if we were able to take statistical records at their face value we should have to conclude that it is a sickness which increases with the spread of material civilization. In civilized States the mortality ascribed to cancer is far greater than among primitive races, and in any one civilized State the mortality now ascribed to cancer is far heavier than a generation ago. The Table (69) of English experience is typical.

Statisticians are, however, a cautious race, and very few of them have been prepared to accept these figures at their face value. Forty years ago King and Newsholme in a very valuable paper initiated a discussion which still goes on. The most striking part of their work was an analysis of the experience of Frankfurt-am-Main, where deaths from cancer had been classified by site of occurrence for many years. It was found that between 1860 and 1889 mortality from cancer of those parts of the body in which the disease was readily detected had not increased. They urged that the general increase of mortality from cancer was consistent with the causal factor being not a greater number of deaths from cancer but a more accurate specification of the causes of death. Twenty-three years later another eminent statistician, Dr. Willcox, of Cornell University, continued the analysis of the Frankfurt data down to 1915, and surveyed the whole field. In his judgment this wider survey confirmed the opinion of King and Newsholme. In his words: "The cumulative evidence that improvements in diagnosis and changes in age composition explain away more than half, and perhaps all, of the apparent increase

TABLE 69  
ANNUAL MORTALITY FROM CANCER (ALL FORMS) PER 100,000 LIVING IN SUCCESSIVE DECADES  
*England and Wales*

	All Ages Standardized	Ages							
		0-	15-	25-	35-	45-	55-	65-	75 and Upwards
<b>MALES:</b>									
1851-60	20.5	1	2	6	18	42	93	150	174
1861-70	25.6	1	2	6	21	54	121	187	227
1871-80	33.3	1	2	7	24	71	159	261	299
1881-90	46.7	2	3	8	30	100	230	376	393
1891-1900	63.5	2	4	10	38	130	316	533	582
1901-10	78.2	2	4	11	41	155	390	668	787
1911-20	89.6	2	4	11	42	168	444	800	973
1921-30	100.4	2	5	12	42	163	472	955	1,276
<b>FEMALES:</b>									
1851-60	43.8	1	2	14	60	128	186	236	233
1861-70	52.1	1	2	16	67	154	230	281	280
1871-80	61.9	1	2	17	79	176	277	352	352
1881-90	73.9	1	3	17	86	205	338	453	460
1891-1900	88.2	2	3	18	89	232	410	583	638
1901-10	94.0	2	2	17	85	232	441	666	790
1911-20	96.0	2	3	16	79	227	438	711	919
1921-30	98.8	2	4	16	76	214	424	774	1,131

in cancer mortality rebuts the presumption raised by the figures, and makes it probable, although far from certain, that cancer mortality is not increasing."

A year or two later, however, Dr. T. H. C. Stevenson recorded in the annual report of the Registrar-General for 1917 the results of some analyses which are not easily reconciled with Dr. Willcox's general conclusion. Dr. Stevenson took for his basis the 685,142 deaths from cancer recorded during 1897-1917 in England and Wales, and inquired whether the increase of mortality were really concentrated upon "inaccessible" or difficult diagnosable sites (see Table 70). As a basis of classification he availed himself of an inquiry made by the Bureau of the Census of the United States of America in 1914. In the United States the practitioners reporting 52,420 deaths from cancer registered in that year were invited to state whether the diagnosis was or was not certain. For the sites classified by Dr. Stevenson as "accessible" the highest proportion of uncertain diagnoses was 0.6 per cent (rectum). In the "inaccessible" group the proportion of uncertainty ranged from 15.3 per cent (ovary and Fallopian tubes) to 72.0 per cent (stomach). Dr. Stevenson found that in the male sex mortality from cancer of "accessible" sites had actually increased faster than mortality from cancer of "inaccessible" sites. The former showed an increase of 56 per cent, the latter of 41 per cent. Among women the position was reversed, but the general increase of mortality from cancer in women was much less than that of cancer in men. "This remarkable and quite unexpected result," wrote Dr. Stevenson, "makes it very difficult to attribute so important a share in the recorded increase in the cancer of males to improved diagnosis as has hitherto seemed probable."

NAWAB SALAR JUNG PARADOUR.

These were the conclusions reached by competent authorities on the evidence available fifteen years ago. Before canvassing them it will be interesting to consider the experience of the last ten years. After the war the male rate of mortality from cancer continued to increase: it was 921 (standardized) per 1,000,000 in 1920, 947 in 1921, and passed the 1,000 in 1925, when it had reached 1,023; then there was a slight decline to 1,018 in 1927, a further rise to 1,032 in 1928, and then practically the same rates 1,031 in each of the following years. The decennial average of

ACCESSIBLE AND INACCESSIBLE SITES OF FATAL CANCER: MORTALITY PER 1,000,000 LIVING 1901-2 AND 1916-17  
*England and Wales*

	All Ages		0	25--	35--	45--	55--	65--	75--	85 and Upwards
	Gross	Standardized								
MALES:										
Accessible { 1901-2	200	211	—	25	—	429	996	1,819	2,380	2,485
1916-17	367	285	—							
Inaccessible { 1901-2	440	461	—	60	—	921	2,373	4,052	4,178	5,512
1916-17	776	598	—	78	—	1,056	2,868	5,521	6,749	8,810
Indefinite { 1901-2	54	55	—	13	—	108	260	369	550	682
1916-17	68	56	—	19	—	115	227	324	429	325
All Sites { 1901-2	694	727	—	98	—	1,458	3,629	6,240	7,108	8,679
1916-17	1,211	939	—	132	—	1,679	4,415	8,354	10,695	13,724
FEMALES:										
Accessible { 1901-2	484	463	4	102	550	1,376	2,064	2,600	3,235	3,962
1916-17	563	486	4	75	500	1,388	2,180	2,951	4,214	5,038
Inaccessible { 1901-2	457	433	11	65	293	937	2,141	3,615	3,857	4,228
1916-17	576	493	11	59	283	950	2,400	4,295	5,493	6,228
Indefinite { 1901-2	45	44	8	13	36	91	155	264	400	687
1916-17	31	28	8	11	23	53	107	160	215	309
All Sites { 1901-2	986	940	23	180	879	2,404	4,360	6,479	7,492	8,613
1916-17	1,170	1,007	23	145	806	2,391	4,687	7,466	9,922	11,575
PERSONS:										
Accessible { 1901-2	347	345	—	68	—	921	1,565	2,253	2,877	3,416
1916-17	480	391	—	78	—	964	1,761	2,754	3,935	4,879
Inaccessible { 1901-2	449	446	—	63	—	929	2,249	3,809	3,991	4,419
1916-17	661	541	—	73	—	1,001	2,628	4,841	5,996	7,080
Indefinite { 1901-2	48	48	—	13	—	99	204	310	463	686
1916-17	47	41	—	14	—	83	165	234	301	314
All Sites { 1901-2	844	839	—	144	—	1,949	4,018	6,372	7,331	8,521
1916-17	1,188	973	—	165	—	2,048	4,554	7,829	10,232	11,973

(Taken from Annual Report of the R.G., 1917, Table LIII.)

1901-10 was 784, so that the rate of 1929 or 1930 had an increase of 31.5 per cent over the average of twenty-five years earlier.

Table 71 (pp. 366-67) gives various details. We cannot without further calculation repeat the analysis of 1917, but, taking the decennium 1911-20 as a datum line and ranking (as in 1917) lip, tongue, mouth and tonsil, jaw, rectum, breast, rodent ulcer, penis, scrotum, other skin, larynx, and testis as "accessible," the remainder, except cancer of bones (which I omit) as "inaccessible" sites, we reach by addition the following results. In 1911-20 the rate for "accessible" sites (males) was 269.3; in 1929 it was 281.5, an increase of 4.5 per cent. In 1911-20 the rate for "inaccessible" sites was 556.1; in 1929 it was 691.4, an increase of 24.3 per cent. The selected causes account for 92 per cent of the total mortality ascribed to cancer in 1911-20, and for 94.3 per cent of the total mortality in 1929. In the last thirteen years the mortality from "inaccessible" cancer has increased much faster than that from "accessible" cancer. This is a very different result from that found by Dr. Stevenson nearly twenty years ago. The figures quoted above are not comparable, because, in order to meet a not very important objection to the usual method, a different method of standardization was used by him. Even the table in the 1917 annual report is not strictly comparable because the sum of the "accessible" and "inaccessible" site rates in 1916-17 has a larger proportion of the total than in our series. Still, the difference is not important enough to invalidate a comparison. These earlier figures showed an increase between 1901-2 and 1916-17 of 35 per cent in mortality from cancer of "accessible" and of a little less than 30 per cent of mortality from "inaccessible" sites. Comparing the complete decennia of 1911-20 and 1921-30, the "accessible" rates are 269.3 and 283.5, an increase of 5.3 per cent. The "inaccessible" rates are 556.1 and 652.5, an increase of 17.3 per cent. It will be noticed that the average rate for the decennium 1921-30 is in the "accessible" group slightly higher, and in the "inaccessible" group decidedly lower, than for the year 1929 used in the last comparison. For 1930 the "accessible" rate was 282.9, the "inaccessible" rate 688.7. It will be felt that these statistical results are a little confusing. While between 1897 and 1917 "accessible" cancer was increasing faster than

TABLE 71

CANCER MORTALITY—RATES PER 1,000,000 POPULATION (STANDARDIZED) FOR THE MORE IMPORTANT SITES FOR EACH SEX, 1901-10, 1911-20, 1921-30, 1926, 1927, 1928, 1929, AND 1930

	All Sites		Lip		Tongue		Mouth and Throat		Jaw	
	Males	Females	Males	Females	Males	Females	Males	Females	Males	Females
1901-10	78.4	94.2	12.8	0.8	43.1	4.4	?	?	22.6	6.9
1911-20	80.7	95.9	12.6	0.7	50.8	4.3	23.5	3.0	25.1	7.2
1921-30	1,004	986	11.5	0.7	46.1	3.8	28.3	3.6	20.8	6.4
1926	1,011	995	10.6	0.6	43.7	3.7	29.6	4.1	21.0	6.9
1927	1,018	984	11.9	1.0	46.6	4.3	29.5	3.4	21.1	6.0
1928	1,032	1,000	12.3	0.7	45.5	4.2	30.5	3.5	19.6	5.5
1929	1,031	999	10.4	0.6	41.8	4.1	27.6	3.5	19.2	6.5
1930	1,031	987	11.3	0.7	40.6	3.5	29.3	3.8	16.7	5.3
	Pharynx		Oesophagus		Stomach		Liver		Gall-bladder	
1901-10	?	?	51.2	14.6	167.2	133.0	?	?	?	?
1911-20	10.8	3.0	60.6	16.5	186.4	139.0	87.1	98.0	6.0	11.6
1921-30	12.6	3.0	64.2	18.1	221.1	155.5	61.0	60.9	8.8	16.6
1926	13.1	3.1	65.4	17.8	222.2	163.2	61.2	59.8	9.1	17.7
1927	13.2	2.8	60.7	18.0	229.0	157.0	55.8	52.1	8.3	17.6
1928	12.6	2.9	64.3	18.7	227.4	161.5	51.8	52.6	9.5	16.9
1929	13.8	2.8	62.3	18.3	237.2	164.6	52.3	50.6	9.4	17.6
1930	11.8	3.2	61.8	18.6	233.7	162.8	47.7	45.4	9.5	17.1
	Mesentery and Peritoneum		Intestine		Rectum		Ovary and Fallopian Tube		Uterus	
1901-10	8.2	15.8	65.3	72.3	79.8	55.9	—	19.2	—	?
1911-20	6.0	12.0	96.8	109.2	93.6	59.3	—	24.3	—	174.4
1921-30	5.4	8.1	125.4	129.9	105.5	59.8	—	36.0	—	157.9
1926	5.6	9.3	131.5	135.4	107.2	59.7	—	35.7	—	156.4
1927	4.8	7.3	132.0	131.8	105.7	60.3	—	38.9	—	155.1
1928	5.8	7.3	132.5	138.5	105.7	58.0	—	39.2	—	154.9
1929	4.4	7.2	134.3	138.6	108.0	58.3	—	40.8	—	150.3
1930	4.9	6.6	136.9	138.4	110.6	59.9	—	42.3	—	143.9

	Breast	Rodent Ulcer	Penis	Scrotum	Other Skin
1901-10	158.4	?	?	—	?
1911-20	170.8	6.7	6.6	2.4	17.6
1921-30	189.1	8.4	6.4	—	17.6
1926	184.3	7.5	6.9	2.7	18.1
1927	193.5	6.5	6.4	3.0	18.8
1928	196.2	9.0	6.1	3.1	18.2
1929	193.7	9.5	5.7	2.7	18.2
1930	194.5	9.1	6.3	2.3	16.1
	Larynx	Lung	Pancreas	Kidney and Suprarenals	Bladder
1901-10	?	10.2	14.5	8.4	?
1911-20	23.9	12.7	16.7	9.1	28.2
1921-30	31.3	25.2	26.3	11.7	30.5
1926	33.5	23.3	26.0	11.4	30.0
1927	31.7	26.8	30.3	12.2	30.5
1928	31.8	32.0	28.8	12.5	32.0
1929	31.4	33.4	30.3	13.2	32.3
1930	31.6	40.2	29.4	13.0	31.8
	Prostate	Testis	Bones	Mediastinum	
1901-10	11.8	?	?	8.1	
1911-20	26.5	4.9	15.7	9.2	4.5
1921-30	47.7	5.8	17.6	12.6	4.6
1926	47.9	5.2	17.3	13.3	5.8
1927	47.8	7.1	18.1	12.9	6.0
1928	53.8	6.3	18.6	13.3	5.4
1929	56.4	5.2	17.6	12.1	5.6
1930	54.9	6.7	17.3	13.1	5.3

(Taken from *Statistical Review of England and Wales for 1930*, Text, Table LII.)

"inaccessible" cancer, during the last decade the relation has been reversed. Is any reconciliation possible?

In connection with the decennial analysis of occupational mortality effected on the material of the census of 1921 and the three years' death certificates of 1921-3, Dr. Stevenson pointed out a very interesting relation between mortality from cancer and social class. The principal facts are shown in Table 72 (pp. 370-71).

These social classes purport to represent the following categories: Upper and Middle Classes form Class I, Intermediates form Class II, Skilled Workers form Class III, Intermediates form Class IV, and Unskilled Workers form Class V. As illustrations of the method of assignment I take first the profession to which some of my readers belong. Physicians, surgeons, registered medical practitioners, and dentists are assigned to Class I; veterinary surgeons to Class II; sick nurses, mental attendants, subordinate medical service (including masseurs, bone setters, and herbalists) to Class III. The reader will recollect that the analysis relates to *men* only. Take now a larger group, that of agricultural occupations. None are assigned to Class I. To Class II are assigned land and estate agents and managers (not auctioneers and estate agents), farmers, farmers' sons or other relatives assisting in the work of the farm, agricultural and forestry pupils (not at colleges), agricultural machine, tractor, proprietors, managers, and foremen. To Class III are assigned gardeners, nurserymen, seedsmen, florists, foresters and woodmen, drainage superintendents, foremen, etc. To Class IV are assigned shepherds, agricultural machine tractor drivers and attendants, agricultural labourers, farm servants, land drainers, drainage labourers, labourers in woods and forests, other agricultural occupations. Class V receives gardeners' labourers, estate labourers, pea and fruit pickers. It would be very easy to recall individual exceptions to this classification. Bone setters have been known to bear titles and to reside in Park Lane, and estate agents to possess Rolls-Royce cars. Yet it would be perverse to deny that, as a statistical grouping, these classes from I to V do correspond to a social-economic trend from the most to the least eligible way of life in terms of the ordinary Englishman's standards of eligibility.

Refer now to the Table. It will be seen that mortality from

cancer in the worst-placed social class is very much higher than in any other class. The difference between Class V and Class IV is greater than between Class IV and Class I. This contrast is much greater for particular sites than for cancer as a whole. Thus the mortality from cancer of the lip in Social Class V is more than five times as great as in Class I, and that due to cancer of the tongue is more than three times as great. On the other hand, cancer of the rectum and anus is little more fatal in Class V than in Class I, and cancer of the colon less fatal.

At the bottom of the Table those sites of cancer which may be called exposed sites, particularly the upper part of the alimentary canal, are grouped together, and it is seen how great is the contrast between Class V and Class I, while for other sites there is no difference. The striking result led Dr. Stevenson and his colleagues to write: "It thus appears that a large proportion, at least, of cancer mortality is of a highly preventable nature, for we must suppose that if the conditions of life of all sections of society could be assimilated to those of its upper ranks, mortality from cancer of the exposed sites would fall for all classes to the Class I level. Indeed, it is very possible that knowledge of the preventable causes accounting for the difference might provide the means of reducing if not eliminating these forms of cancer for all causes,\* for these causes might well be found to apply in varying degree to all sections of society." (Report, p. xxi.)

I shall not discuss this view now, except with respect to the particular statistical issue which is perplexing us. If we believe, as I think we must, that during the last thirty to fifty years the general conditions of life of the population have improved greatly, so that the contrast between the extent of *commoda vitae*—whether quality and quantity of food, clothing, fresh air, or what one pleases—enjoyed by Classes I and V is much less than a century ago; this, then, might account for the recent stagnation or even decrease in mortality from cancer of exposed sites. Let us think for a moment of the beginning of the alimentary canal, fatal cancers of which are less frequent than before the war. I was taught that non-specific predisposing causes of, for instance, cancer of the tongue were a chronically septic mouth, the irritation due to a jagged tooth, a clay pipe, etc. One was also taught that syphilis

\* The quotation is exact but perhaps for "causes" we should read "classes."

TABLE 72

STANDARDIZED MORTALITY (C.M.F.) AT AGES 20-65 YEARS OF ALL OCCUPIED AND RETIRED CIVILIAN MALES AND OF THE FIVE SOCIAL CLASSES FROM CANCER OF VARIOUS SITES, 1921-23

Standardized Mortality (C.M.F.)							
	Occupied and Retired	I	II	III	IV	V	
1. All sites .. .. .	128.4	102.5	118.1	127.1	123.8	157.8	
Lip .. .. .	1.0	0.3	0.5	0.7	1.4	1.7	
Tongue .. .. .	7.5	3.6	5.5	7.1	7.5	12.4	
Mouth .. .. .	2.2	1.3	1.6	2.2	2.2	3.6	
Jaw .. .. .	3.2	0.9	2.3	3.1	3.5	5.2	
Tonsil .. .. .	1.6	0.4	1.4	1.5	1.7	2.6	
Pharynx .. .. .	1.8	1.6	1.4	1.8	1.8	2.9	
Oesophagus .. .. .	9.7	7.4	8.8	10.1	8.5	12.6	
Stomach .. .. .	29.5	17.6	24.2	29.4	31.2	38.2	
2. Small Intestine .. .. .	0.6	0.7	0.6	0.7	0.6	0.8	
Caecum .. .. .	0.9	1.1	1.1	1.0	0.7	0.8	
Hepatic and Splenic Flexures .. .. .	0.4	0.1	0.5	0.3	0.5	0.3	
Sigmoid Flexure .. .. .	2.2	3.4	2.5	2.2	1.8	2.1	
Colon, part not stated .. .. .	5.7	7.5	6.2	5.6	5.0	5.7	
Intestine, part not stated .. .. .	3.4	2.8	3.6	3.4	3.4	3.6	
Large Intestine .. .. .	9.1	12.0	10.2	9.1	7.9	8.8	
Total Intestine (excluding rectum) .. .. .	13.3	15.4	14.2	13.2	12.0	13.2	
Rectum and Anus .. .. .	12.5	11.6	12.8	12.7	12.0	12.2	
3. Larynx .. .. .	4.6	3.3	4.4	4.3	4.4	6.2	
Skin .. .. .	3.0	1.9	2.2	3.0	3.6	4.5	
Breast .. .. .	0.2	—	0.3	0.2	0.2	0.4	

	Peritoneum, Omentum, Mesentery	0.9	1.3	0.8	1.0	0.9	0.9
4.	Pancreas .. ..	3.4	3.5	3.5	3.3	3.0	3.8
	Kidney and Suprarenal .. ..	1.6	1.1	1.7	1.6	1.5	1.4
	Bladder .. ..	3.1	3.3	3.0	3.2	2.4	3.9
	Prostate .. ..	2.9	3.2	3.2	3.0	2.3	2.5
	Testes .. ..	0.9	0.8	1.5	0.8	0.8	0.7
	Brain .. ..	0.5	0.8	0.8	0.6	0.4	0.3
	Bones .. ..	2.2	1.6	2.5	2.3	2.1	1.9
	Gall-bladder .. ..	0.9	0.9	0.8	1.0	0.8	0.9
	Lung .. ..	3.3	3.3	3.6	3.2	2.6	4.1
	Liver .. ..	8.8	6.2	8.9	8.7	8.8	9.5
	Abdomen .. ..	0.6	0.7	0.5	0.6	0.6	0.6
	Neck .. ..	0.3	0.6	0.1	0.3	0.4	0.6
5.	Lymphatic Glands .. ..	4.1	3.6	3.4	4.2	3.6	5.6
	Mediastinum .. ..	1.9	3.6	2.1	1.7	1.9	1.8
	Other specified sites .. ..	2.0	2.6	2.1	2.0	1.7	2.5
	Multiple .. ..	0.2	0.3	0.2	0.2	0.1	0.2
	Site not stated .. ..	0.1	—	0.1	0.1	0.1	0.1
	1. Upper Alimentary Canal .. ..	56.8	33.0	45.6	56.0	57.8	79.3
	2. Intestine and Rectum .. ..	25.8	27.1	27.1	25.9	24.0	25.4
	3. Larynx, Skin, Breast .. ..	8.1	5.1	6.7	7.9	8.3	11.4
	4. Deep-seated sites .. ..	16.4	16.5	17.8	16.7	14.2	16.3
	5. Miscellaneous and ill-defined sites .. ..	21.2	20.8	20.9	20.8	19.8	24.9
	1, 3. Exposed sites .. ..	65.0	37.9	52.3	63.9	66.1	90.9
	2, 4, 5. Other sites .. ..	63.3	64.3	65.8	63.4	57.9	66.5

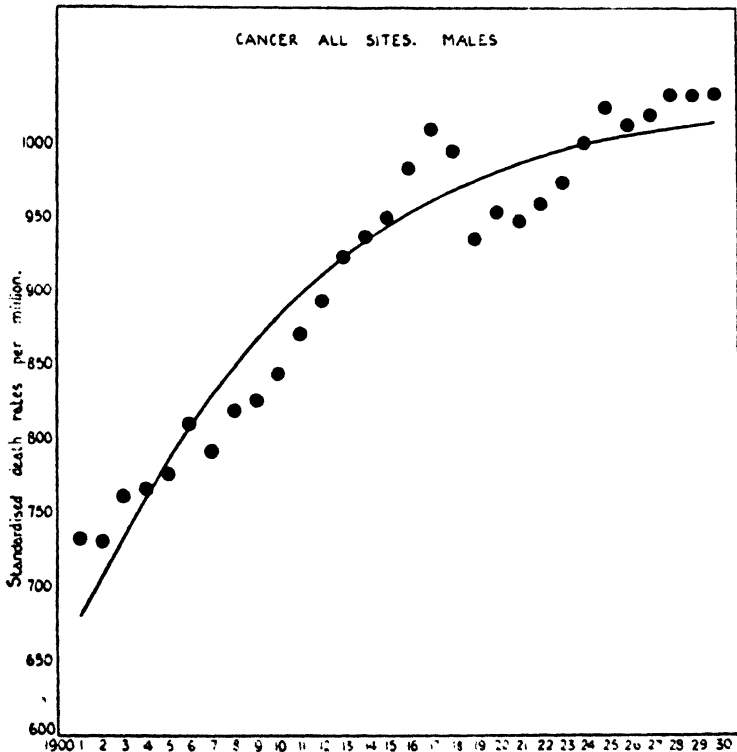
(Annual Report of the R.G. Decennial Supplement, 1921. Occupational Mortality, p. xxiii, Table 4.)

with an associated glossitis was an important precursor. That splendid teacher, the late H. L. Barnard, used to tell us in out-patients that it might be all very well to smoke and all very well to get syphilis, but that a prudent man contented himself with one or other enjoyment, for their combination might lead to cancer of the tongue. I suppose it is not too optimistic to believe that in the last generation mouths have become cleaner, prophylactic dentistry commoner, the smoking of foul pipes and the suffering from ill-treated syphilis decidedly rarer than in the past. We must add, although—for reasons to be given later on—it is not, perhaps, a factor of numerical importance yet, that the surgical and radiological treatment of malignant disease of these sites has steadily improved. But, at any rate within the terms of the passage I have just quoted from the report on Occupational Mortality, the facts that mortality from cancer of the stomach is increasing and that cancer of the stomach is one of the forms of cancer of an exposed site for which the contrast in mortality between Class I and Class V is very great are unfavourable to the optimistic explanation of the previous paragraph. It will be seen that with the help of statistical analysis and starting from plausible aetiological hypotheses, one reaches results interesting but incomplete. At this point it will be convenient to recur to the purely statistical aspects of the matter.

Waiving for the moment the question whether rates of mortality from year to year are materially comparable, can we from examination of the secular graphs of mortality make any reasonable guess as to the future trend? The graph of age standardized mortality among males certainly does suggest a slackening rate of increase, but he would be a bold man who would prophesy the value of the rate of mortality which will be ultimately attained. Across the chart (Graph 8) has been drawn the locus of a function, the simple logistic function, which has often proved a good means of describing the evolution of biological processes, such as the growth of population. It will be seen that, although not so bad a representation of the general trend, it certainly does not describe the "law" of change. The equation of this particular curve is:

$$y = \frac{1,027 \cdot 6}{1 + e^{-\frac{(3 \cdot 376 + t)}{8 \cdot 074}}}$$

where  $y$  is the annual rate of mortality in year  $t$  (origin 1901). It postulates a rate of mortality never in finite time attaining 1,027.6 per 1,000,000. In each of the years 1928-30 (inclusive) the attained rate was higher than this. I think we may have a good deal of faith that the standardized mortality-rate in our genera-



GRAPH 8.

tion will not exceed 1,050, and that it will certainly not increase fast. But we cannot be more precise than that.

The course of mortality in females is still more refractory to any mathematical polishing process. It is, indeed, a strange picture, suggesting some queer speeding up of the rate of increase just before the war, leading to a falling away which has been replaced by a fairly steady or at worst slightly increasing trend. Mainly owing to the facts that the mortality from cancer in women is not increasing, or at least is only very slowly increasing,

while the mortality in males is now definitely greater than in females, most people seem to be more interested in doing sums with the data for males. But from the educational point of view the mortality from cancer in women is more interesting. At the present time more than a third of the whole mortality from cancer in women is accounted for by recorded primary cancers of the breast or uterus, and these rates for sites which lend themselves to relatively easy diagnosis have changed greatly in the present generation. In 1901, when the all-sites rate was 943 per 1,000,000 (these are age standardized rates), the rate for the breast was 148.9 and for the uterus 223.8. In 1930, when the general rate was 987, the breast rate had risen to 194.5 and the uterus rate had fallen to 143.9. Yet, as one knows, the operative treatment of cancer of the breast is one of the triumphs of modern surgery, a much less dangerous and more successful treatment than that of the uterus—in spite of great improvements in the latter field.

Up to a certain point the explanation of this change is adequate. It was shown first by the late Dr. T. H. C. Stevenson that the death-rate of single women from cancer of the breast was much higher and from cancer of the uterus much lower than that of married women.

Since his original demonstration of the broad facts it has been shown that the higher incidence of fatal cancer of the breast is correlated with incomplete functioning of this sexual organ, i.e. that those who do not become pregnant have a greater liability. It has been shown that the higher liability of married women to uterine cancer is confined to cancer of the neck of the uterus, and that this liability does not increase with the number of children born, although associated with the bearing of children, i.e. that the contrast is between parturients and women who have borne no children. Some writers have even gone so far as to say that multiparae are more favourably situated than women who have only borne one or two children.

Further, it has been shown that, even now, the number of women suffering from malignant disease of either organ who present themselves at so early a stage of the morbid process that really radical surgery can be used is a disappointingly small proportion. Hence, although we should expect treatment already to

influence rates of mortality we should not be surprised to find that the effect is still but small.

All this is satisfactory enough to anybody who likes explanations, but there is a good deal left wholly unexplained. For instance, if we make comparison between countries on the same cultural level, and compiling statistics with equal accuracy, we find very great differences between the rates of mortality from cancer of the breast and uterus.

TABLE 73

## FEMALES

*Cancer Mortality of the Genital Organs and Breast. Rates per 10,000*

Year	Genital Organs			Breast		
	England and Wales	Italy	Holland	England and Wales	Italy	Holland
1905	—	1·50	1·29	—	0·57	0·80
1906	—	1·63	1·24	—	0·59	0·89
1907	—	1·59	1·24	—	0·56	1·03
1908	—	1·57	1·43	—	0·57	0·89
1909	—	1·56	1·28	—	0·59	0·97
1910	—	1·60	1·40	—	0·58	1·00
1911	2·43	1·48	1·17	1·84	0·55	0·98
1912	2·46	1·40	1·27	1·97	0·59	1·19
1913	2·55	1·50	1·40	2·02	0·59	1·08
1914	2·50	1·51	1·31	1·99	0·59	1·10
1916	2·47	1·49	—	2·11	0·56	—

Tables 73 and 74 comparing the experiences of England and Wales and the Netherlands (with some other countries) bring this out. Here we have two countries suffering not widely dissimilar tolls of total mortality from malignant disease, yet contrasting greatly in respect of cancer of the female breast and sexual organs. An expert committee of the Health Organization of the League of Nations spent much time and labour in seeking to explain this discrepancy. The investigation verified the facts; it made it clear that no simple explanation (such as better facilities, or better use of facilities, for radical treatment) was adequate, and it got no further. If we could explain this discrepancy we should, I imagine, be near the centre of the

TABLE 74

CANCER MORTALITY AT AGES EXPRESSED AS RATES PER 10,000

	50-60					60-70					70 and Upwards				
	England and Wales	Sweden	Holland	Italy	Prussia	England and Wales	Sweden	Holland	Italy	Prussia	England and Wales	Sweden	Holland	Italy	Prussia
1911 { Male	27.85	23.88	37.48	15.36	25.58	59.52	52.63	97.26	30.67	52.34	87.87	70.27	100.47	42.91	62.74
1911 { Female	31.85	22.27	34.73	19.64	25.98	55.64	43.10	77.44	33.57	46.68	83.50	59.43	96.45	48.23	58.06
1912 { Male	28.35	22.41	37.77	14.06	24.36	60.63	54.24	95.20	31.08	53.57	91.93	65.89	97.61	43.20	67.61
1912 { Female	33.37	23.08	37.98	19.33	25.44	56.63	42.35	77.80	31.82	46.60	87.39	60.04	92.59	45.15	60.13
1913 { Male	28.62	23.27	36.89	14.88	24.42	63.31	50.61	97.98	31.65	54.77	92.86	67.84	112.59	45.26	65.68
1913 { Female	33.65	23.05	35.19	20.18	26.66	60.04	45.85	81.72	32.46	47.32	86.84	61.69	94.41	46.02	60.77
1914 { Male	28.68	24.54	35.87	15.47	23.67	63.98	52.04	98.51	31.08	54.33	97.06	71.39	103.43	48.15	65.85
1914 { Female	33.36	24.57	35.05	19.58	25.69	58.84	44.32	78.34	33.30	47.27	88.03	68.95	101.52	46.85	85.58
1915 { Male	28.99	25.04	36.68	—	23.70	62.20	53.12	97.52	—	53.38	95.00	76.25	113.36	—	62.05
1915 { Female	33.34	23.04	33.70	—	24.08	58.85	45.50	83.23	—	45.41	86.60	68.34	95.74	—	54.98
1916 { Male	28.66	24.03	32.86	15.77	23.55	63.71	54.49	104.62	30.64	50.95	95.85	75.72	112.85	47.07	65.95
1916 { Female	33.43	23.39	35.96	20.23	25.51	58.79	45.94	81.41	31.89	45.00	86.97	67.35	113.76	47.27	41.75
1917 { Male	29.11	24.00	34.75	15.38	22.89	63.58	58.39	102.22	29.70	47.01	100.12	73.61	118.18	45.38	61.59
1917 { Female	34.05	25.05	36.01	19.29	24.39	59.97	46.26	83.12	31.53	43.41	89.79	61.31	100.90	46.21	57.13
1918 { Male	29.25	—	34.70	—	23.63	62.44	—	101.10	—	50.78	93.86	—	108.17	—	60.51
1918 { Female	33.19	—	35.02	—	24.86	59.81	—	85.34	—	44.74	88.17	—	111.94	—	56.06

cancer maze. That we cannot is a warning to those who would solve the problems of malignant disease from an arm-chair. I suppose to most readers this is an unsatisfactory account. We seem to know a little about a great many things of importance and a great deal about a few things of no special importance, but the epidemiological-statistical method has, so far, reached no clear-cut conclusion which is of general aetiological importance. That is, I think, a just criticism, yet I am not pessimistic.

The answer to the young lady's question to Babbage, of calculating machine fame: "Please, Mr. Babbage, if you ask the wrong question, will it give you the right answer?" is still "No." Even in this country approximately accurate statistical data of mortality from cancer are a product of less than a generation. The accuracy is still only approximate.

\*            \*            \*            \*            \*

Here my sketch of crowd-diseases must end. A great many important objects have been brought into the picture, but many have been omitted.

Among crowd-diseases in the grand manner, malaria does not yield in importance to plague; among crowd evils always with us, whooping-cough is not less deadly than measles, while traffic accidents (which surely come within my definition of a crowd-disease) are a good deal more deadly. The trouble is that when one enlarges the definition of epidemiology one is theoretically committed to a treatise on *all* the bad habits of mankind, and so must practise an illogical moderation.

Perhaps, however, enough has been said to enable an interested reader to go further by himself. I hope to have taught him that this is a field of study not only as important but as interesting as others universally agreed to be within the circle of general culture. The subject is one which the non-professional reader has no excuse for neglecting on the ground that it is dry and technical. If and when all educated persons are as familiar with this kind of medical history as they are with political history, the level of discussion of social legislation will be raised and less attention

will be paid to the dicta of "experts," "well-known Harley Street specialists," or even "professors," to the benefit of all concerned.

#### RECOMMENDATIONS FOR FURTHER STUDY

My "Review of Recent Statistical Studies of Cancer Problems" (*Cancer Review*, March 1928) gives a slightly fuller account and numerous references. I advise the student to read, *first*, the discussions of cancer statistics printed in the annual reports of the Registrar-General, beginning with that contained in the report for 1911.

# INDEX

- Abingdon, isolation hospital at, responsible for spread of scarlet fever, 224
- Accessory food substances, lack of, in diet of Millbank Penitentiary prisoners, 114
- Accidents, minor, in a projectile factory, cause of incidence of, 132
- Adults—  
     healthy, basal metabolism of, biometric study, 102, 103  
     influx of, into manufacturing districts, effect on mortality returns, 50
- Aertryckal infection in mice, resemblance to coli-typhoidal illnesses in man, 76
- Africa, original home of smallpox, 227
- Air-temperature, mean—  
     in week before date of registration of death, correlation of mortality-rate from in weeks before date of registration of death, 66  
     in week before date of registration of death, correlation of mortality-rate from respiratory diseases with, 66
- Airs, Waters, and Places—  
     theme of, explained, 19  
     treatise on, by Hippocrates, 18
- Alastrim—  
     origin of, 242  
     type of infection in Geelong, 234
- Allbutt, Sir Clifford, 25
- Amar, energy requirements of various grades of work deduced from statistics of, 104
- Analysis, methods of, all selective, 66
- Andral, 351
- Aneurysm, mortality from, 337, 338
- Annuities, purchase and sale of, how rendered a legitimate business operation, 44, 45
- Anti-cholera—  
     inoculation in Second Balkan War (1913), results examined, 96  
     prophylaxis, value of, 171
- Anti-smallpox vaccination—  
     circumstances in which beneficial, and in which of little value, 75  
     results of dermal changes produced by, on smallpox fatality, 96, 97
- Anti-typhoid inoculation, 87  
     among 17th Lancers, average number of men protected and unprotected by inoculation, 92  
     circumstances in which beneficial and in which of little value, 74, 75  
     during the Great War, 87 et seq.  
     comparative statistics among protected and unprotected men tabulated, 88  
     criticism of, 89, 90
- Anus, cancer of, fatality of, generally distributed over all social classes, 369
- Arabists, advance of mathematics under, 29
- Aristotle, 25  
     conception of man as an ensouled body, 128
- Attack-rate of disease against which immunization is practised, not constant, 81, 82
- Attack-rates upon inoculated and uninoculated compared, 83
- Augustine of Hippo, St., 128, 131
- Australia—  
     smallpox in, 228 et seq.  
     vaccination in, 228
- Avicenna, 29
- Bacillus aertrycke*—  
     herd of mice infected with, mortality-rates, oscillations of, 72, 73  
     infection due to, concerned with experimental epidemiology, 69  
     infection, resistance of herd of mice among non-immunized and immunized entrants compared, 73, 74  
     *See also* Aertryckal infection

*Bacillus typhosus*, 137

Bacon compared with Plato, 39

Bacteriological and experimental research, positive results of, 61, 62

Bag schema, assumption of, in comparing samples of inoculated and uninoculated, 82

Bagehot, Walter, criticism of Dickens' method of describing social evils, 126

de Baillou, Guillaume, 35, 51, 211  
contribution to knowledge of epidemiology made by (1640), 33, 34

personal interest in his patients exhibited by, 34

Balkan War, Second (1913), anti-cholera inoculation in, results examined, 96

Ballonius. *See* de Baillou

Baltimore—

death-rates from smallpox, vaccinations and vaccination rates, tables of, 232, 233

smallpox in—

history of, 236

morbidity and mortality (1882-1883), table of, 237

Banks, Sir Joseph, 257

Barnard, H. L., on syphilis and smoking as precursors of cancer of the tongue, 372

Baron, 246, 248

Basal metabolism of healthy adults, biometric study of, 102, 103

Batavia, hygienic conditions of, 170

Bateman, 212

Batley, smallpox epidemic (1891-92)—  
attacks and recoveries among vaccinated and unvaccinated compared, 283

proportion of recoveries among vaccinated and unvaccinated, 284

Bedfordshire, death-rate from phthisis, 348

*See also* England and Wales

Benedict and Cathcart, measurements of energy transformations of trained cyclist (heat production and work), 100, 101

Benedict and Harris, biometric study of basal metabolism of healthy adults, 102, 103

Beri-beri—

etiology of, difficulty in solving, 115  
food-deficiency disease, 110

Berlin Lazaretto, fatality of smallpox epidemic (1871-72), enormous percentage reached, 285

Bernouilli, James, 145

Bernouillis, the, 47

Bills of Mortality, 180

collection to 1752, 47

discontinuance of (1849), 41

disregarded by Sydenham, 41

institution of (1532), 40

issued by special printing press (1625), 41

Biological group opposed to views of both medical and humanitarian groups regarding tuberculosis, 353, 354

Biometric study of basal metabolism of healthy adults, 102, 103

Biometricians—

controversies with field epidemiologists and public health officers, 64, 65

mistakes of, 65

pioneer work of, 63

Birmingham, mortality of, decline in since 1811, 50

Blane, Sir Gilbert, prevalence of consumption among young adults, 347, 349

Body lice, conveyance of typhus by, 174

Boerhaave, 38

Bolton and Reading, economics of, compared, 121

Bolton, Northampton, Reading, Warrington—

comparison of death-rates from all causes per 1,000 persons (1911-13), 120

mortality-rates from all causes expressed in terms of Reading (1911-13), 121

Bolton-upon-Dearne—

typhoid fever epidemic at (1921), 56, 160

due to polluted water supply, 161, 162

- Bowley, A. L., economics of Reading, Northampton, Bolton, and Warrington, 121
- Bradford, smallpox epidemic (1893)—  
attacks and recoveries among vaccinated and unvaccinated compared, 283  
proportion of recoveries among vaccinated and unvaccinated, 284
- Brazil—  
smallpox in, 242  
two epidemics of typhoid in, not of water-borne origin, 159
- Breast, cancer of, death-rate from of single women much higher than that of married women, 374
- Breath of life and the body, relation between, 128
- Breeding from stocks, resistance to specific infection, effect on epidemic herd-illnesses, 76, 77
- Bretonneau, 200
- Broadstairs and Uppingham, differential preventive treatment of acute poliomyelitis at, 313, 314
- Broadwater—  
time- and space-distribution of typhoid fever cases (March-December 1893), 151, 152  
typhoid fever epidemic at. See Worthing
- Bronchitis, mortality-rates, male and female, ages 45-55, 55-65 (1901-10), England and Wales, Lancashire, Northants, Cumberland, Westmorland, 119, 120
- Brown, Capt. A. J. See Davy, Major P. C. T.
- Browne, Sir Thomas, indifference to various views regarding the psyche, 129, 130
- Brownlee, John, 53, 54, 172, 276, 302, 303  
on Farr's views regarding origin of epidemic prevalences, 53  
on results of dermal changes produced by vaccination with smallpox fatality, 97
- Brownlee, John (*cont.*)—  
periodicity in relation to epidemics of measles, 191
- Budd, William, 140, 228  
report of cases of typhoid fever, proving origin of the outbreak by means of the *materies morbi*, 140-143  
researches on typhoid fever commended by Sir John Simon, 144
- Buhl (Pettenkofer-Buhl) law explained, 60
- Bureau of the Census of the United States of America, inquiry regarding cancer mortality, 363
- Burke, Edmund, 78  
remark of, in paper on food scarcity, quoted, 109
- Caius, John—  
false views on epidemiology held by, 32  
on the short duration of English sweat, 32  
*Treatise on the English Sweat* (1552), 31
- Calorie requirements of standard "man," investigations into, 107
- Calories—  
expended per square metre by bearers of marching load in post-absorptive state and after meals, tabulated, 102  
greater number required by father of family doing heavy muscular work, 107  
respectively required by the respective members of a family, tabulated, 106
- Calorimeter, expensiveness of, 105
- Calorimetry, indirect dexterity required in, 105
- Cancer—  
increase with spread of civilization, 361  
infectivity of, no reason for supposition of, 361

**Cancer (cont.)—****mortality—**

among women, variability in course of, 373

annually per 100,000 living in successive decennia, England and Wales, table showing, 362

England and Holland, male and female compared (1911-18), 375, 376

in United States, "accessible" and "inaccessible" sites compared, 363

large proportion preventable, 369  
question of increase from improvement in diagnosis, 361, 363

statistical data only approximate, 377

mortality-rate (standardized) among males, forecast as to figures likely to be reached in present generation, 372, 373

mortality-rates per 1,000,000 population for the more important sites for each sex (1901-10, 1911-20, 1921-30, 1926, 1927, 1928, 1929, 1930, tabulated, 366, 367

occurrence at Frankfurt-am-Main, 361

cases classified by site, 361

of "accessible" and "inaccessible" sites, mortality compared, 363, 364, 365

of various sites, mortality (standardized), of all occupied and retired civilian males and of the five social (1921-23), 368, 369

tabulated, 370, 371

**Carbohydrates**, nutrition of body by, 100

**Carrier-infection**, character of typhoid prevalence due to, 17

**Carriers—**

human, of cholera, disease kept alive by, 171

life-long, of diphtheria, 207

of diphtheria. *See* Diphtheria, carriers of

transmission of typhoid fever by, 158

**Cathcart, E. P.—**

on calorie requirements of standard "man," 107

and Orr, calories expended per square metre by bearers of marching load, tabulated, 102

*See also* Benedict and Cathcart

**Cerebro-spinal fever—**

carrier-rate in, constituting epidemiological event, 311

dates of outbreaks of in Europe, 310, 311

first outbreak of occurring in Geneva (1805), 310

over-crowding factor in, 311

**Cerebro-spinal meningitis**, diagnosis of by Matthey (1805), 310

**Chadwick, E.**, non-professional advocate of measures of suppression of tuberculosis, 353

**Chance—**

events, hypotheses regarding, how usually illustrated, 64

hypotheses about, numerical appraisements based on, 64

**Chaplin, Arnold**, 48

**Chess**, game of, Galen's system of epidemiology compared to, 26, 28

**Children**, infectious diseases specially peculiar to, 137

**Children's pilgrimages**, epidemics of, 133

**Chingford**, cases of paratyphoid fever at, 163

**Cholera—**

as epidemic phenomenon confined to Asia, 168

epidemics of—

a factor in the institution of a State health department, 54

before nineteenth century, 165

exotic character of, 165

in early nineteenth century—

dispersiveness of, 165, 166

causes, 166

infection, man the reservoir of, 171

outbreak of, in England in 1831, 166

- Cholera (cont.)**—  
 pandemics of, routes taken by, 166, 167  
 quarantine measures against, of doubtful value, 72  
 relation to typhoid group of illnesses, 137
- Cicero**, 69  
 low estimate of Greek physicians at Rome held by, 25
- Civilian males**, occupied and retired, mortality (standardized) from cancer of various sites (1921-1923), tabulated, 370, 371
- Civilization**—  
 gross physical demands on energy useless under present system of, 107  
 spread of, increase of cancer with, 361
- Clarke, Sir James**, obtained post for William Farr in General Register Office, 51
- Cleanliness**, ordinary, neglect of, and outbreaks of epidemic disease, correlation between, first exposition of, 54
- Cleek makers**, seven, average weekly expenditure of food among families of, 108
- Clifton College**—  
 influenza pandemic at (1918)—  
 numbers attacked in summer and not attacked in autumn, 86  
 numbers not attacked in summer and attacked in autumn, 86
- Climatic factors**, variations of effect of, on variations of severity of plague, 307
- Clinical medicine**, contribution of Hippocrates to, 18
- Coal-mines**, explosions in, variability of annual deaths due to (1887-1906), 82
- Coggeshall (Essex)**, diphtheria epidemic at, 198
- Coin-tossing**, group and individual prognosis in, contrasted, 16
- Coli-typhoid infection in man**, resemblance of aertryckal infection in mice to, 76
- Collins, Wilkie**, *The Woman in White* (quoted), 174
- Colon**, cancer of, less fatal in lower classes than in uppermost class, 369
- Common necessities**, total deficiency of in diet of Millbank prisoners, 112
- Compositors**, mortality from tuberculosis, above normal, general mortality normal, 359
- Constitutions**, materials for in form, 51
- Consumption**—  
 death-rate from in London within the Liberties (1629-1835), 347  
 progressive increase of—  
 knowledge derived by Woolcombe from mortuary records of Holycross (near Shrewsbury) (1750-1800), 345, 346  
 Woolcombe's method of demonstration, 345, 346  
*See also* Phthisis; Tuberculosis, pulmonary
- Contagion**—  
 doctrine of, difference between Galen and Fracastori as regards, 59  
 views on, expressed by Fracastori, 32, 33
- Contagium vivum***, 53  
 first suggestion of transmission of disease by (Fracastori), 58
- Copeman, S. Monckton**, experimental production of cowpox, 272
- Corfield, Professor W.**, on origin of typhoid epidemic at Maidstone (1897), 148, 158, 159
- Cornwall**. *See* Devonshire and Cornwall
- Coroner's jury**, verdict on death of prisoner at Millbank Penitentiary, 112
- Cowpox**—  
 absolute preventive of smallpox, Jenner's view, 261  
 experimental production of, 272  
 inoculation with, immunity to smallpox conferred by, 253

- Cowpox** (*cont.*)—  
 inoculation, value of, in prophylaxis, 248  
 naturally acquired, immunity to smallpox conferred by, 253  
 sufferers from, rendered insusceptible to smallpox, 245  
 "true" or "spurious," differentiation of, 262
- Crawford**, quantitative study of nutrition, 99
- Creighton, C.**, 226, 241, 248, 249, 250, 251, 258, 260, 261, 271, 275  
 account by, of typhus in England in first quarter of nineteenth century, 178  
 account of measles by, 181  
 and Jenner, E., 245-273  
 characteristics of, 248  
 cholera as a new disease, 165  
 exposure of Jenner by, 268, 270  
 importance of soil-changes in causation of cholera, 169  
 indifferent attitude of, towards bacteriology, 60  
 on hypothesis of plague, 267  
 on results of dermal changes produced by vaccination on smallpox fatality, 96, 97  
 writings of, 266
- Cromwell, Thomas**, institution of Parish Registers at order of, 40
- Crookshank, E. M.**, 262
- Crookshank, F. G.**—  
*First Principles and Epidemiology* (quoted), 61, 62  
 opinion as to the nature of English sweat, 31
- Crowd-diseases**, aetiology of, psychological determinant in, 133, 134
- Crowd** point of view primary in epidemiology, 103
- Crowds** industrially employed, mortality of, 117 et seq.
- Culpin, M.**, demonstration of psychological differentiation of victims of telegraphist's cramp as a group, 131
- Cumberland**, mortality-rates from pneumonia and bronchitis, male and female, ages 45-55, 55-65 (1901-10), 119, 120
- Cumpston**, 228, 231
- Dancing mania**, epidemics of, 133
- Darwin**, 53, 249
- Davy, Major P. C. T.**, and Brown, Capt. A. J., outbreak of typhus in Serbia during the Great War, 175, 176
- Death**, registration of, correlation of mortality-rate from respiratory diseases with air-temperature in week before date of, 66
- Death-rate**, general, as distinct from specific, 52  
*See also* under names of diseases
- Deaths**, observed, as percentages of expected deaths in occupational groups, 124, 125
- Dermal changes** produced by vaccination, results on smallpox fatality, 97
- Desire**, first idea of, 127
- Devonshire and Cornwall**, severe outbreak of poliomyelitis (1911), 312
- Dewsbury**—  
 smallpox epidemic (1891-92)—  
 attacks and recoveries among vaccinated and unvaccinated compared, 283  
 proportion of recoveries among vaccinated and unvaccinated, 284
- Diarrhoea** (summer), decline in former prevalence of, 172
- Dickens, Charles**, method of describing social evils criticized by Walter Bagehot, 126
- Diet**—  
 determination first by plain necessity, 116  
 epidemiological aspects of, 98 et seq.  
 investigation by family budget method, 106, 107

Diet (*cont.*)—

- of prisoners at Millbank Penitentiary, 111
- tabulated and analysed, 113, 114
- qualitative factors of, stress laid upon, 115, 116
- secondary factors operating in, 116
- Dietetic experiments, failure of, instanced, 110

Diets—

- family, investigation of, difficulties attendant upon, 105, 106
- of 154 families, results of investigation of, 107
- qualitative factor of, important, 115
- rich in vitamins, doubt as to control of herd-illness by, 77
- supposed to be adequate, illness produced by, 110

Diphtheria—

- affecting children mainly, 137
- age of attack, statistics, 199
- and scarlet fever, frequency of epidemics compared, 205
- carriers of—
  - experiments relating to, 207
  - life long, 207
  - time-relations of, 206, 207
- causes of spread of, 198
- death-rate (standardized), male and female (1861-1924), with differences (male and female (1861-1924), 215
- distribution of immunity in group in Royal Naval School at Greenwich, 208

epidemic—

- at Coggeshall (Essex), 198
- at Pirbright (Surrey) (1883), 198
- at Radwinter (Essex) (1876), 198
- in England, incidence of in rural districts and in towns compared, 198
- in Europe, mortality of, compared with that of scarlet fever, 197
- in Great Britain, increase, importance of in middle of nineteenth century, 197
- in schools of different social classes, differences in evolution of, 208

Diphtheria (*cont.*)—

- natural and heritable resistance to, differences of, 208
- occurrence of, in days of Roman Empire, 197
- outbreaks of, means of prevention of, 209
- prevention by immunization, 209
- Schick test of resistance to, 205, 208
- school infections of, 199
- seasonal trend of, 205
- whooping cough, measles, scarlet fever, death-rates in quinquennial periods under 15 years, 181
- Disease-prevalence, secular variations of, description yet wanting, 62
- Döring, 211
- Dudley, immunization of part of a group in diphtheria, 209
- Dutch, scientific appreciation of problem of recrudescence of foot-and-mouth disease, 71, 72

Dysentery—

- and tuberculosis, mortality from, in mental hospitals compared, 344
- decrease in London, false statement regarding, 46
- outbreak of, among prisoners at Millbank Penitentiary following change for the worse in diet, 112

Earthquake of Lisbon (1756), 178

Ectromelia—

- infection due to, concerned with experimental epidemiology, 69
- virus, almost total immunity secured from in herd of mice, 75

Efficiency—

- ambiguity of expression, 108
- measure of, how obtained, 109

Einstein, 69

- Emotional reactions, individual and crowd, characterizing ages of transition, 130

**Empirics, the—**

era of, 23, 24

rule of ("Tripod of the Empirics"),  
24**Encephalitis lethargica—**and "epidemic constitution" of  
influenza, relation between,  
315, 316

statistics, 317

**Endemic—**diseases of different places, dis-  
similarity of, observed by  
Hippocrates, 18and epidemic diseases, distinction  
between, made by Hippo-  
crates, 18**Energy—**daily quantum of, necessary to feed  
population of thirty million  
"men," 108requirements of various grades of  
work tabulated, 104transformations of trained cyclist,  
series of exact measurements  
of, 100, 101use, less gross physical demands  
on, under present system of  
civilization, 107**England—**much typhus and little typhoid in  
at end of eighteenth century,  
139

smallpox in, 242

typhus in, during first quarter of  
nineteenth century, 178, 179and Holland, cancer mortality, male  
and female, compared (1911-  
1918), 375, 376and Sweden, mortality rates, males  
and females, ages 10-54  
(1901-10), 117, 118, 119**and Wal-**cancer mortality annually per  
100,000 living in successive  
decennia, table showing, 362death-rates from measles, scarlet  
fever, diphtheria, and  
whooping cough, in quin-  
quennial periods, under 15  
years, 181decline in mortality from phthisis  
from 1860 onwards, 349**England and Wales (cont.)—**London, Bedfordshire, Lan-  
cashire, Sussex, comparative  
death-rates from phthisis,  
348mortality from tuberculosis an-  
nually, 345mortality rates from pneumonia  
and bronchitis, male and  
female, ages 45-55, 55-65  
(1901-10), 119standardized mortality per  
1,000,000 living from syphilis  
and diseases of syphilitic  
origin (1911-28), 337, 338typhoid fever in (1871-1931)—  
effect on of gradual purification  
of water supplies, 158standardized death-rates at all  
ages (1870-1931), tabulated,  
156, 157**English—**medical authors, want of clearness  
in writing, a defect of, 62**sweat—**clinical characteristics of, 31  
heavy mortality among young  
people, 326modern, identification with in-  
fluenza, 31sweats, sixteenth-century epidemics,  
in relation to influenza, 320**Epicurus, 128****Epidemic—**actual, link in chain of epidemio-  
logical happenings, 321

constitutions of Sydenham, 36

disease, outbreaks of, correlation  
with neglect of ordinary  
cleanliness, 54diseases, changes in, noted by  
Sydenham, 36happenings, "laws" of, difficulty of  
finding through statistical  
method applied to data of  
human recorded experience,  
67

prevalences, immediate causes of, 53

**Epidemics—**as self-regulating phenomena  
capable of biological descrip-  
tion, 306

**Epidemics (*cont.*)—**

- immediate course of, description still needed, 62
- stamping-out of, when only practicable, 70, 71

**Epidemicity, circulation of non-immunes a necessary condition of, 76**

**Epidemiological treatment of codified material, 52**

**Epidemiologists—**

- indispensability of statistical method in work of, 17
- practical, study of psychology important for, 134
- and physicians, standpoint of, with regard to typhoid fever, contrasted, 15

**Epidemiology—**

- contribution to, by Sydenham, 36, 37
- contribution to knowledge of, made by de Baillou (1640), 33, 34
- crowd point of view primary in, 103
- crux of, illustrated by influenza, 137
- definition of, 15
- etymological meaning of, 15
- experimental, 68 et seq.
  - advantages of, 68, 69
  - art of, 68
  - bacterial infection and virus infection concerned with, 69
  - employment of mice for, 68, 69
  - method in, application of, 60
  - and human, simile used to express relation between, 69
- failure in advance of, principal cause, 21
- field observers in, controversy with biometricians, 64, 65
- foundations of, laid by Hippocrates, 21
- history of, preceding introduction of statistical method, 17 et seq.
- partaking no share in development of mathematical development, 29
- persistence of Galen's theories regarding, 28, 29
- pragmatic, a characteristic of the mid-Victorian period, 56
- precision of language important in describing phenomena of, 62

**Epidemiology (*cont.*)—**

- problems of, still awaiting solution, 65
- progress of, lacking in medical profession during eighteenth century, 47
- research in, prerequisite of, 46
- study of, relation of work of William Farr to 51, 52
- system of, devised by Galen, compared to game of chess, 26, 28
- wrong system of, devised and promulgated by Galen, 26

**Epping, paratyphoid fever epidemic at (1931), due to infected milk supply, 162, 163**

**Error, normal curve of, 280, 281**

**Eton College—**

- influenza pandemic at (1918)—
  - numbers attacked in summer and re-attacked in autumn, 86
  - numbers not attacked in summer and attacked in autumn, 86

**Europe, Western, cholera in, 165**

**Events and premonitions, probability of observed concurrence of, 81**

**Exeter jail, outbreak of typhus among foreign prisoners in reign of Elizabeth, cause of, 175**

**Expectation of life, partial or limited, use of, in comparing resistance of mice to herd evils, 73**

**Explosions in coal-mines, variability of annual deaths due to (1887-1906), 82**

**Families—**

- diets of, investigation of, difficulties in, 105, 106
- distribution of measles in St. Pancras epidemic (1926), 185
- supported by State or municipality, physiological circumstances of, need investigation, 108

**Family—**

- budget method of investigation of diet, 106, 107
- calories respectively required by the several members of, tabulated, 106

- Famine, connection of typhus with, 178, 179
- Farmer, demonstration of psychological differentiation of victims of telegraphist's cramp as a group, 131
- Farr, Samuel—  
 edition of Hippocrates, epidemiological treatises by (1780), 47  
 no allusion to medical statistics by, 47
- Farr, Thomas, on immediate causes of epidemic prevalences, 53
- Farr, William, 49, 50, 51, 190  
 appointed compiler of abstracts in General Register Office, 51  
 death-rates from consumption in London within the Liberties (1629-1835), 347  
 gross rate of smallpox mortality on children in Glasgow, 182, 183  
 importance of life tables to students of preventive medicine, 45  
 kind of problems dealt with in his epidemiological work, 52  
 no information from, regarding evolution of epidemics, 53  
 opinion regarding immunization against one type of disease only, 53  
 organizer of medical statistics, 51  
 qualities of, compared with those of Simon, 54, 145, 146  
 relation of his works to study of epidemiology, 51, 52  
 scarlet fever mortality of children in Liverpool, 214
- Fatality-rate of disease, against which immunization is practised, not constant, 81, 82
- Fatality-rates, explanation of, 83
- Fats, nutrition of body by, 100
- Filth, propagation of typhoid fever by, belief in, 144
- First and Third Books of Epidemics*—  
 by Hippocrates, 18  
 description of the four *Constitutions* in, 19
- Flies, part played by, in spread of cholera, 170
- Flu—  
 investigations into cholera by, 169  
 statistics of incidence of cholera, 169
- Food—  
 or drink, primary aetiological factor of cholera and typhoid, 165  
 shortage of certain articles of, in areas of maximum production, 122
- Food-deficiency, qualitative, symptom-complexes due to, 110
- Food-stuffs, sophistication of, 115
- Foot-and-mouth disease—  
 outbreaks of—  
 extinction by slaughter, when only available, 71  
 recrudescence after apparent extinction of outbreaks, reason for suggested, 71  
 re-importation, 71  
 virus of, intensification by passage through a non-immune, possibility of, 71, 72
- Foreest, Peter, 35
- Fourier, 190
- Fox, Charles James, primary cause of death of, 116
- Fracastori, 35, 53, 138  
 coinage of word *syphilis* by, 58  
 diagnosis of typhus by, 173, 174  
 first suggestion of transmission of disease by *living* contagium, 58  
 scientific intuition possessed by, 32  
 views on contagion expressed by, 32, 33  
 and Galen, difference between, as regards the doctrine of contagion, 59
- France—  
 much typhoid and little typhus in, at end of eighteenth century, 139  
 Southern, departments of, outbreak of cholera in (1884), 167
- Frankfurt-am-Main, analysis of cases of cancer occurring at, 361
- Freud, opposition to dynamic psychology of, 130

- Galen, 17, 18, 35, 268  
 abilities of, 25  
 character of, 25  
 knowledge of treatment of tuberculosis possessed by, 344  
 opposition to the view of man's conscious reason being paramount, 129  
 persistence of his theories regarding epidemiology, 28, 29  
 self-revelations of, 25  
 system of epidemiology devised by, compared to game of chess, 26, 28  
 translation of his most important works into Latin by Linacre, 31  
 wrong system of epidemiology devised and promulgated by, 26  
 and Fracastori, difference between, as regards the doctrine of contagion, 59  
 and Hippocrates, distance of time between, 24  
 Galton, Sir Francis, 28  
 pioneer in statistical methodology, 63  
 and Pasteur, age of, 58 et seq.  
 Garthshore, Dr., 261  
 Garvin, J. L., 131  
 Gas analysis, dexterity required for, 105  
 Gauss-Laplace function, 53  
 Gendrin, 351  
 General principles, importance of conclusion of an argument from, 62  
 General Register Office, establishment of, 51, 54  
 German medical authors, want of clearness in writing, a defect of, 62  
 Glasgow—  
 measles in, periodicity of, 188, 189  
 mortality from smallpox and measles in children compared, 182, 183  
 periodicity of measles in, 188, 189, 191  
 Glasgow (*cont.*)—  
 smallpox epidemic (1900-1)—  
 attacks and recoveries among vaccinated and unvaccinated compared, 283  
 proportion of recoveries among vaccinated and unvaccinated, 284  
 tenement housing in, generating measles at early age, 194  
 Glossitis and syphilis as predisposing causes of cancer of the tongue, 369, 371  
 Gloucester—  
 smallpox epidemic (1895-96)—  
 attacks and recoveries among vaccinated and unvaccinated compared, 283  
 proportion of recoveries among vaccinated and unvaccinated 284  
 Gonorrhoea—  
 estimation of number of persons likely to acquire, 339  
 percentages of infection in Hamburg and in Switzerland compared, 340  
 Goodall, E. W., non-complication of other infectious diseases with influenza, 37, 38  
 Gordon, Mervyn, 272  
 Graunt, John, 39, 40, 42, 43, 51, 54  
 criticism of sources employed by, 45, 46  
 elected Fellow of the Royal Society, 43  
 epidemiological importance of, 48  
 first demonstration of facts of vital statistics by, 43, 44  
 life table of, 45  
 merit and defect of his life table, 45  
 work on vital statistics, 47  
 republished, 47  
 Great War, the—  
 anti-typhoid inoculation during, 87 et seq.  
 comparative statistics among protected and unprotected men tabulated, 88  
 epidemic of tuberculosis in mental hospitals of England and Wales during last years of, 342, 343

- Great War, the (*cont.*)—  
 increase of venereal disease due to barbarism coincident with 340  
 mortality from pulmonary tuberculosis increasing during, 349  
 prevalence of cerebro-spinal fever in, 311
- Greek physicians—  
 at Rome, low estimate of, held by Cicero, 25  
 extent of knowledge of tuberculosis, 344
- Greek Sanitary Corps, results of anti-cholera inoculation in, 96
- Greeks, Ancient, of first century A.D., intellectual self-sufficiency of, 24, 25
- Greenwich. *See* Royal Naval School, Greenwich
- Greenwood, M., and Yule, U., on results of anti-cholera inoculation in Greek Sanitary Corps, 96
- Group-prognosis, how differing from individual prognosis, 16
- Haeser, H., 25, 60  
 on psychical plagues (*Psychische Seuchen*), 133  
 opinion on the writings of de Baillou (*Ballonius*), 35
- Haileybury College—  
 influenza pandemic at (1918)—  
 numbers attacked in summer and not attacked in autumn, 86, 87  
 numbers not attacked in summer and attacked in autumn, 86, 87
- Halley, 47  
 on life table constructed from deaths alone, 45
- Halliday, J. L., prejudicial effects of tenement housing on generating measles, 194
- Hamburg—  
 percentage of infections of syphilis in, 339
- Hamburg (*cont.*)—  
 percentage of gonorrhoeal infection in, 340  
 serious outbreak of cholera in, in 1802, 167
- Hamer, Sir William, 28, 38  
 criticism of theory of transmission of typhoid fever by "carriers," 158  
 on periodicity in measles, 187  
 opinion as to the nature of English sweat, 31
- Harrison, Col. L. W., on relaxation of propaganda against venereal diseases, 340
- Harrow School—  
 influenza pandemic (1918)—  
 numbers attacked in summer and re-attacked in autumn, 86  
 numbers not attacked in summer and attacked in autumn, 86
- Harvey, W., 17
- Hawkins, Francis Bissett, 51  
 treatise on medical statistics, 49
- "Heart," first idea of, 127
- Heart, disorderly action of, admission of medical importance of psychic factor in, 130
- Heat—  
 mechanical equivalent of, discovery of, 99  
 production in relation to work performed, experiments tabulated, 100, 101
- Heberden, William, 51, 138  
 revival in medical statistics exhibited by monograph of, 49  
 (the younger), errors in medical statistics committed by, 45, 46
- Hecker, 31
- Henle, Jakob, contribution to epidemiology made by, 58, 59
- Herd-illness—  
 epidemic—  
 doubt as to control of, by diet rich in vitamins, 77  
 effect on, of breeding from stocks resistant to specific infections, 76, 77  
 protection of herd against, by immunization, single-handed, doubtful, 79

- Herd-illness (*cont.*)—  
 evolution of, what dependent upon, 76  
 intensity of, need of measuring the balance of the several factors determining, 76
- Herd immunity, level of, modification and study of, 62
- Hill, A. Bradford, principal factors in causation of tuberculosis in the printing industry, 359
- Hippocrates, 17, 25, 46, 51, 52  
 a student of preventive medicine and epidemiology, 18  
*Books of Epidemics*, edition by Samuel Farr (1780), 47  
 contribution to clinical medicine, 18  
 distinction between endemic and epidemic diseases made by, 18  
 first description of epidemic mumps given by, 20, 21  
 first description of malaria, 23  
 foundations of epidemiology laid by, 21  
 hypothesis of humours of the body, 22  
 observations on weather in relation to prevalence of disease, 23  
 and Galen, distance of time between, 24
- Hippocrati  
*corpus*, books comprising, 18  
 methods of research modernized by Pettenkofer, 60
- Hirsch, 60
- Hirst, Fabian, 300
- Holker, 167
- Holland, Sir Henry, *Medical Notes and Reflections*, 58
- Holland and England, cancer mortality, male and female, compared (1911-18), 375, 376
- Holycross (near Shrewsbury), progressive increase of consumption (1750-1800) at, derived from mortuary records of parish by Woolcombe, 345, 346
- Howard, 228  
 on history of smallpox in Baltimore (quoted), 238
- Humanitarian school—  
 views regarding—  
 cause of decline of tuberculosis, 353  
 prevention of tuberculosis, 353
- Humours of the body, doctrine of, 22
- Hungary, relatively unurbanized mortality from tuberculosis high, 355
- Hunter, John, Jenner a pupil of, 247
- Hutchinson, Sir Jonathan, 255
- Huxham, 48, 174  
 clinical difference between putrid fever (typhus) and slow nervous fever (typhoid), described by, 138
- Ill-health, factors upon which dependent, according to Galen, 26
- Illness, sudden prevalences of, formulation of laws describing their emergence, 46
- Immunization—  
 against some diseases wholly efficient, 75  
 artificial—  
 of man, 78 et seq.  
 question of diminution by—  
 of risk of dying of a disease if contracted, in comparison with those not immunized, 79, 80  
 of risk of taking a disease if exposed to it in comparison with those not immunized, 79, 80  
 in prevention of diphtheria, 209  
 single-handed, protection of herd against herd-sickness doubtful, 79
- Industrial—  
 crowd, units of, earlier and easier breakdown in later life, 122
- Fatigue Research Board, investigation into telegraphist's cramp (1927), 131
- life—  
 comparative mortality in, 117 et seq.  
 in towns, depression of, 123

- Infancy, high mortality-rate in, first demonstration, 43  
 Infant mortality, general reduction in, 125  
 Infectiousness, statistical measure of, 184, 185  
 Infectivity of diseases, proof of, 185  
 Influenza—  
   aetiology of, difficulties of, 323  
   and "English Sweats," relationship between, 31, 320  
   crux of epidemiology illustrated by, 137  
   epidemics of existing, for over two hundred and fifty years, 320  
   mortality from, since pandemic of 1918-19, 326-328  
   non-complication of other infectious diseases with, 37, 38  
   pandemic, 1918-19—  
     age mortality from, 325  
     at four great public schools—  
       numbers attacked in summer and re-attacked in autumn, 86  
       numbers not attacked in summer and attacked in autumn, 86  
     believers in portents of, 39  
     havoc wrought by, 326  
     high mortality from second wave, 180  
     no great emotional impression created by, 326  
     practical definition of, 320  
 Influenzal period, five stages of, 323, 325  
 Ingenhousz, J., expresses doubt of Jenner's inoculation, 260  
 Ingrassia (of Palermo), 211  
 Inoculated and uninoculated—  
   attack-rates upon, compared, 83, 84, 85  
   minimum test to be applied to, 82, 83  
   question of differentiation, 82, 83  
   samples compared, 80  
     with samples of black and white counters, 80  
 Inoculation—  
   advantageousness and effectiveness, compared, 83, 84  
   Inoculation (*cont.*)—  
     results of, fallacies regarding, 84, 85, 86  
   Intestinal lesions, cholera and typhoid determined by, 165  
   Ireland, shortage of certain articles of food in, in areas of maximum production, 122  
   Isolation Hospital, Abingdon, responsible for spread of scarlet fever, 224  
 Jenner, E.—  
   apprenticeship of, 246  
   becomes President of Royal Jennerian Institute, 263  
   birth of, 246  
   case of smallpox, patient vaccinated by him ten years previously, 264  
   death of, 265  
   doubt expressed as to his inoculations, 260  
   elected Fellow of Royal Society, 247, 250  
   in Berkeley, 251  
   in Cheltenham, 251  
   in London, 362  
   merits and demerits of his character summed up, 287  
   obtains degree M.D.—  
     Oxford, 263  
     St. Andrews, 251  
   publishes "An Inquiry into the Causes and Effects of the Variolae Vaccinae," 252  
   pupil of John Hunter, 247  
   view that cowpox was an absolute preventive of smallpox, 261  
   work on—  
     calcification of coronary arteries, 248  
     cuckoo, 249  
     method of preparing tartar emetic, 248  
     temperature of hedgehog, 248  
   writes "An Inquiry into a Disease known in Gloucestershire by the name of Cowpox," 251  
   and Creighton, C., 245-273

- Jenner, Sir William, passage quoted illustrating his knowledge of group difference between typhus and typhoid, 139, 140
- Johnstone, James, *Malignant Epidemical Fever of 1756 in the Town of Kidderminster*, 178
- Jorge, Ricardo, 242
- Joule, discovery of the mechanical equivalent of heat, 99
- Jurin, 226
- Juvenal, 25
- Karn, Mary N. *See* Stocks, Percy, intensive study of history of measles in St. Pancras
- Katastases* of the atmosphere as a factor in producing ill-health, 26, 27
- Katastasis* of Hippocrates, 19, 20  
     explanation of, 20
- Kaye, John. *See* Caius
- Kidderminster, outbreak of typhus in, in 1756, 178
- Kilburn and St. John's Wood, outbreak of throat illness in, 201
- King and Newsholme, Sir A., analysis of deaths from cancer at Frankfurt-am-Main, 361
- Koch, R., 266  
     demonstration of unity of tuberculosis as a pathological process, 351  
     isolation of virus of tuberculosis by,
- Laboratory experiments, criticism of, by upholders of statistical methodology, 63, 64
- Labour, moderate and severe, energy requirements of respectively, tabulated, 104
- Laennec, 351
- Lancashire—  
     death-rate from phthisis, 348  
     *See also* England and Wales  
     mortality-rates from pneumonia and bronchitis, male and female, ages 45-55, 55-65 (1901-10), 119, 120
- Lancers, 17th, incidence of typhoid fever on (Meerut, 1905-9), 90, 91, 92, 93, 94
- Latham, P. M., *An Account of the Disease lately prevalent at the General Penitentiary* (1825) (quoted), 111, 112
- Latin, translation of Galen's works into, by Linacre, 31
- Lavoisier, 116  
     doctrine determining a nutritional policy first enunciated by, 98, 99  
     and Seguin, demonstration that the consumption of oxygen increased as the amount of manual work done increased, 98, 99
- Lefèvre, results tabulated of requirements of sedentary workers under different conditions, 103
- Leicester—  
     smallpox epidemic (1892-93)—  
         attacks and recoveries among vaccinated and unvaccinated compared, 283  
         proportion of recoveries among vaccinated and unvaccinated, 284
- Lenz, F., prognostication as to numbers of persons likely to acquire syphilis, 339
- Liebig, quantitative study of nutrition by, 99
- Life assurance, contracts of, purchase and sale of, how rendered a legitimate business operation, 44, 45
- Life table—  
     constructed from deaths alone, 45  
     first construction upon correct lines, 45
- Life tables, value to students of preventive medicine, 45
- Linacre, Thomas, translation of Galen's most important works into Latin by, 31
- Lind, 48
- Lip, cancer of, greatest prevalence in lowest social classes, 369

- Lisbon, Earthquake of (1755), 178
- Liverpool—  
 mortality of, decline in, since 1811, 50  
 scarlet fever mortality of children in, 214
- Living contagion. *See* *Contagium vivum*
- Lobstein, 351
- Lodge, Thomas, 268
- Logic, practical issues not determined by, 78
- London—  
 boroughs—  
 death-rate from tuberculosis, diminishing according to wealth, increasing according to poverty, 356, 357, 358  
 grouped according to wealth, mortality of, table illustrating, 356, 357, 358  
 death-rate from phthisis, 348  
*See also* England and Wales  
 death-rates (annual) per 1,000,000 from measles (1852-1901), 104  
 decrease of dysentery in, false statement regarding, 46  
 measles epidemic of 97 weeks' smallpox in, 239  
 smallpox epidemics (1892-93, 1901, 1902)—  
 attacks and recoveries among vaccinated and unvaccinated compared, 283  
 proportion of recoveries among vaccinated and unvaccinated, 284  
 within the Liberties, death-rate from consumption in (1629-1835), 347
- Lottery prize, chance of obtaining, compared with chance of infectivity with measles, 185, 186, 187
- Louis, 351
- Low, Bruce, 297
- Lucretius, belief in mortality of both soul and body, 128
- Luxmoore, Capt., report upon incidence of typhoid fever upon 17th Lancers (Meerut, 1905-9), 90-95
- Lycanthropy, epidemics of, 133
- Macaulay, comparison of Plato and Bacon as philosophers, 39
- McCollum and Simmonds, *The Newer Knowledge of Nutrition*, 4th edition, 1929 (quoted), 115
- McCulloch, *Statistical Account of the British Empire* (containing Farr's paper on London death-rate for consumption), 347
- Macdonell, W. R., social status and vaccination, 276
- McGrigor, Sir James, changes for the worse in diet of prisoners at Millbank Penitentiary sanctioned by, 111
- Maidstone—  
 epidemic of typhoid fever at (1897), 17, 146  
*See also* Typhoid fever
- Maintenance cost, variability of, discussed, 102, 103
- Malaria, first description of, by Hippocrates, 23
- Male births, excess of, first demonstration, 43
- Males—  
 higher post-natal mortality-rate of, first demonstration, 43  
 standardized mortality-rate from cancer among, 372, 373
- Malingering, ailments for which no "organic" basis could be found laid to charge of, 130
- Mal-nutrition, fatal results of, in prisoners at Millbank Penitentiary, 112
- Malthus, 51
- Malton, typhoid fever epidemic (1932) due to polluted water supply, 162
- Man, artificial immunization of, 78 et seq.

**Manchester—**

- mortality of, progressive decline in, 49, 50
- smallpox epidemic (1892-93)—
  - attacks and recoveries among vaccinated and unvaccinated compared, 283
  - proportion of recoveries among vaccinated and unvaccinated, 284

**Manchuria—**

- epidemic of—
  - plague in, infection from tarbagan causing, 308
  - primary pneumonic plague in, mortality in, 307

**Manufacturing towns, diminished mortality why not always real, 50**

**Marching load, bearers of, calories expended by, per square metre, in post-absorptive state and after meals, tabulated, 102**

**Married and single women, respective death-rates from cancer of the breast and uterus contrasted, 374**

**Mass hysteria, epochs of special onset, 130**

**Mass phenomenon, doctrine of disease as, studied by Hippocrates, 18**

***Materies morbi*, re-importation of, 71, 72**

**Mathematics—**

- advance of, under Arabists, 29
- development of, not shared by epidemiology, 29

**Maximum production, shortage of certain articles of food in areas of, 122**

**Measles—**

- affecting children mainly, 137
- and atmospheric pressure, relation between, 193
- and scarlet fever, mortality compared, 183
- and smallpox, mortality from, compared in children in Glasgow, 182, 183
- and tuberculosis compared, 351

**Measles (*cont.*)—**

- attack of, followed by life-long immunity, 183
- course of, traceable from seventeenth century, 180
- death-rates (annual) from, in London (1852-1901), 184
- epidemic of—
  - in 1807-8, high infant mortality from, statistics of, 182
  - in London in 1674, 181
  - in London of 97 weeks' period, 191
  - St. Pancras (1926), distribution in families, 185
- epidemiological phenomena of, explanation of, 193
- exposure to infection of, resulting in some degree of immunity, 183
- generated at early age by tenement housing in Glasgow, 194
- in ancient times, 180
- in St. Pancras (1916-28), intensive study of, 192
- infection from, periodicity very short, 183, 187
- infectiousness of—
  - increased, and meteorological factors, relation between, 193
  - variations in, 193
- infectivity with, chance of, compared with chance of obtaining lottery prize, 185, 186, 187
- periodicity of, 183
  - in Glasgow, 191
  - in Sheffield, 191
  - reasons for, 195
- personal infection from, 186
- postponement of age of attack, importance of, 195
- prevention of attack of, at early age, plans for, 194
- scarlet fever, diphtheria, and whooping cough, death-rates in quinquennial periods under 15 years, 181
- second attacks excessively rare, 75
- susceptibles to, in relation to increasing and decreasing attack-rate, 187, 188

- Medical group, views regarding the cause of decline of tuberculosis, 353
- Medical profession, lack of epidemiological research among, during eighteenth century, 47
- Medical Research Council, special reports on calorie requirements of standard "man," 107
- Medical research into aetiology of tuberculosis summarized, 351
- Medical statistics—  
defective, 50  
eighteenth-century contributions to, 47  
English, comparatively brief period over which extending, 65, 66  
revival of interest in, at close of eighteenth century, 49  
treatise on, by F. B. Hawkins, 49  
work of, organized and revolutionized by W. Farr, 51
- Meerut, typhoid fever epidemic among 17th Lancers (1905-9), 90, 91, 92, 93, 94
- Mendel, Kurt, on occupational cramps (quoted), 131
- Meningococcus carrier, dangers of, in overcrowded dormitories, 312
- Mental hospitals—  
mortality (primary and secondary) from dysentery and tuberculosis compared, 343  
of England and Wales, epidemics of tuberculosis in, during last years of Great War, 342, 343
- Mice—  
advantages of employment in experimental epidemiology, 68, 69  
aertryckal infection in, resemblance to coli-typhoidal infection in man, 76  
herd of—  
almost total immunity to *Ectromelia* secured in, 75  
epidemic in, how rendered persistent, 70  
healthy immigrants to, 70
- Mice (*cont.*)—  
herd of (*cont.*)—  
how established, 70  
infected with *Bacillus aertrycke*—  
mortality from specific infection, why not declining to near zero, 73  
mortality-rates in oscillations, 72, 73  
mortality-rate of those infected, how varied, 70  
mortality-rates according to seniority, 72  
originally infected members, 70  
reactions to condition under which living, 72  
resistance to *Bacillus aertrycke* infection among non-immunized and immunized immigrants compared, 73, 74
- Pasteurella* infection in, analogy with influenza or diphtheria, 76
- Mid-Victorian period, pragmatic epidemiology a characteristic of, 56
- Military life, effect of, on cerebro-spinal epidemics, 312
- Milk, contaminated, important mechanism in spread of diphtheria, 198
- Milk supply, infected—  
cause of paratyphoid epidemic at Epping (1931), 162, 163  
cause of paratyphoid outbreak at Walthamstow (1931), 163  
one probable cause of throat illness in Kilburn and St. John's Wood, 203-205
- Millard, Killick, 243
- Millbank Penitentiary—  
diet of prisoners in, 111, 113, 114  
grave results of change in, 111, 112  
prisoners confined in, 110, 111
- Milne, first construction of life table upon correct lines by, 45
- Mind-body relation, 133
- Miners' nystagmus, 133
- Minimum test to be applied to inoculated and uninoculated, 82, 83

- Modern life, "strain" and "pace" of, 122
- de Moivre, 47
- Moore, J., 265
- Morbidity—  
 rather than mortality, present tendency to concentrate research on, 126  
 research in, importance from point of view of preventive medicine, 126
- Mortality—  
 levelling down of, how indicated, 125  
 variations of, difficulty of accurate expression in terms of variations of related measures, 67
- Morton, 138
- Moscow, Napoleon's retreat from, high mortality from typhus among troops, 177
- Mumps, epidemic, first description of, by Hippocrates, 20, 21
- Munich—  
 typhoid fever at—  
   causation, 158, 159  
   deaths from (1851-73, 1851-1906), 149  
   prevalence, alleged cause of, 150
- Munk, W., 256
- Murchison, Charles, non-belief in doctrine of the *materies morbi* as agent in spread of typhoid fever, 140, 143
- Murray, J. A., 226, 227
- Napoleon I (the Great)—  
 changed views regarding, in the times of our great-great-grandparents, 130  
 outbreak of typhus during retreat of his army from Russia (1812), 177  
 sickness among troops during invasion of Russia by, 177
- Nervous fever, slow. *See* Typhoid fever
- Nervous system, central, epidemic diseases of, 310
- Netherlands, Royal Commission on epidemics of foot-and-mouth
- New South Wales—  
 smallpox in, 228  
 first record of, 228
- New York, outbreak of acute poliomyelitis in, statistics, 315
- Newsholme, Sir A., and King, analysis of deaths from cancer at Frankfurt-am-Main, 362
- Nightingale, Florence, humanitarian views of, 353
- Non-immunes, circulation of, a necessary condition of epidemicity, 76
- Normal curve of error, 280, 281
- Northampton—  
 death-rate, excessive (ages 15-25), largely due to tuberculosis (footnote), 120  
 Bolton, Reading, Warrington, comparison of death-rate from all causes per 1,000 persons (1911-13), 120  
 Bolton, Warrington, Reading, mortality-rates from all causes expressed in terms of Reading (1911-13), 120, 121  
 Life Table, construction of, 45
- Northamptonshire, mortality-rates from pneumonia and bronchitis, male and female, ages 45-55, 55-65 (1901-1910), 119, 120
- Notifiable diseases, routine practice of Medical Department of Ministry of Health in relation to, 328, 329
- Nutrition—  
 biochemical study of, 98  
 experimental investigation of, difficulties of, 105  
 qualitative appeals of, increase in literature dealing with, 110  
 quantitative and physical study of, 98, 99  
 study of, science a measurement in, 100
- Nystagmus, miners', 133
- Occam's canon (law of parsimony), 278

- Occupations—**  
 analysis of mortality in (Registrar-General's), 123, 124  
 fourteen groups with mortality from tuberculosis more than twice that of all occupied and retired males, 358, 359
- Old Bailey, outbreak of typhus among persons in court in 1750, 176**
- Order-of-dying-out—**  
 explanation of, 44  
 how constructed, 44  
*See also* Life tables
- Orr. *See* Cathcart and Orr**
- Osborne, Ethel, and Vernon, H. M.,**  
 cause of incidence of minor accidents in a projectile factory, 132
- Overcrowding—**  
 domestic, influence on incidence of an infectious disease, difficulties in ascertaining, 66  
 effect of, on mortality from scarlet fever, 220
- Over-eating and over-drinking, deaths from, 116**
- Paracelsus, 35**
- Paralysis, general, of the insane, mortality from, 337, 338**
- Parasyphilitic diseases, mortality from, 337, 338**
- Paratyphoid fever—**  
 cases at Chingford, 131  
 epidemic, Epping (1931), due to infected milk supply, 162, 163  
 outbreak at Walthamstow (1931) due to infected milk, 163
- Pariset, E., 267**
- Parish Clerks, Company of, obtain decree to set up printing press for issue of Bills of Mortality, 41**
- Parish Register:**  
 collated by Thomas Short, 40  
 English, institution of, 40
- Parsimony, law of (Occam's canon), violation of, 278**
- Pasteur, 53**  
 and Galton, age of, 58 et seq.
- Pasteurella—***  
 infection due to, concerned with experimental epidemiology, 69  
 infection in mice, analogy with influenza or diphtheria, 76
- Paul, St., of Tarsus, 25, 131**
- Paytherus, 261**
- Pearson, George, 255, 262, 271**  
 on smallpox inoculation, 256
- Pearson, Professor Karl—**  
 criticism of statistics of anti-typhoid inoculation by, 95, 96  
 forecast regarding the death-rate of tuberculosis, 354, 355  
 on results of dermal changes produced by vaccination on smallpox fatality, 97  
 pioneer in statistical methodology, 63
- Pellagra, food-deficiency disease, 110**
- Pepys, Sir Lucas, 263**
- Percival (of Manchester), 48, 49**
- Periodicities, objective, 190**
- Periodicity—**  
 concealed, method of searching data for, 190, 191  
 in measles, 187 et seq.
- Periodogram analysis, 190**
- Pettenkofer—**  
 modernization of Hippocratic methods of research by, 60  
 on cause of typhoid fever in Munich, 150, 158, 159  
 on soil contamination as cause of prevalence of typhoid fever at Munich, 150
- Pettenkofer-Buhl doctrine of cholera, 168**
- Pettenkofer-Buhl law. *See* Buhl (Pettenkofer-Buhl) law**
- Petty, Sir William, 43, 54**
- Phthisis. *See* Tuberculosis, pulmonary**
- Physicians and epidemiologists,**  
 standpoint of, with regard to typhoid fever, contrasted, 15
- Pirbright (Surrey), diphtheria at (1883), 198**
- Pitt, William (the younger), primary cause of death of, 116**

- Plague, 289 et seq.  
 atmospheric and climatic conditions  
   in relation to, 300  
 bubonic—  
   epidemic of, at Rome during  
     time of Galen, 25  
   no man-to-man infection of,  
     reason for, 380  
 epidemics, number of deaths  
   recorded in Bills of Mor-  
   tality, 40  
 epidemiology of, 299  
   achievements illustrating, 61, 62  
 extermination of, 345  
 extinction of, in a town, reasons  
   for, 307  
 history of, 289  
   in England, 291  
   in London, 291  
 in Burma, 296  
 in China, 296  
 in East Anglia (1906-18), 291-293  
 in Gujrat, statistics of, table of, 303  
 in Hoshiarpur, statistics of, table of,  
   301, 302, 303  
 in India, 295  
   mortality of, 297  
 in nineteenth century, 294  
 in Thibet, 296  
 interval of epidemic of, longer than  
   solar year, 306  
 massive infection with; certain  
   atmospheric conditions re-  
   quired for, 306, 307  
 mortality in India, graph of, 298  
 mortality of, in world during 1930,  
   excluding Asia, 299  
 pandemic of 1896, 294  
 pandemics of, 290  
 pneumonic—  
   mystery of, 308  
   primary, clinical diagnosis of, 307  
   special example of pestilence, 137  
   transmission of, from rat to man,  
   299  
   variations of severity of, and varia-  
   tions of climatic factors,  
   relation between, 307  
 Plato, 25, 131  
   compared with Bacon, 39  
   conception of the relation between  
   the psyche and the body, 128  
 Pliny, the Elder, advocacy of open-air  
   treatment of tuberculosis by,  
   344, 345  
 Pneumonia—  
   and influenza, relation between,  
   329, 330  
   mortality-rates, male and female,  
     ages 45-55, 55-65 (1901-10),  
     England and Wales, Lan-  
     cashire, Northants, Cumber-  
     land, Westmorland, 119, 120  
   primary, compulsory notifiable  
   disease, 328  
 Poels on possible cause of recrudescence  
   of foot-and-mouth  
   disease, 71, 72  
 Poliomyelitis, acute—  
   minor importance of familial in-  
   fection, 314  
   prevalence of, climatic, 313  
   schools at Broadstairs and Upping-  
   ham, differential preventive  
   treatment at, controversy  
   relating to, 313, 314  
   severe epidemic of, in 1926, 312, 313  
   severe outbreak of, in Devonshire  
     and Cornwall in 1911, 312  
 Post-Jennerian controversy, 274-288  
 Poverty—  
   as a primary factor in the aetiology  
   of tuberculosis, sole occupa-  
   tion showing, 358, 359  
   mortality from tuberculosis a mea-  
   sure of, 356, 357, 358  
 Power, W. H.—  
   diphtheria epidemics at Radwinter  
   (Essex) and Pirbright (Surrey), 198  
   report on outbreak of throat illness  
   in Kilburn and St. John's  
   Wood (1878), 201  
 Pre-immunization, value of, con-  
   flicting opinions as to, 74, 75  
 Premonitions and events, probability  
   of observed concurrence of,  
   81  
 Preventive medicine—  
   importance of research on mor-  
   bidity from point of view of,  
   126  
   students of, value of life tables to,  
   45

- Price, constructor of Northampton Life Table, 45
- Pringle, 48, 176
- Printing industry, prevalence of tuberculosis in members of, principal factors in causation, 359
- Prisons, apportionment of individual rations in, result of, 103
- Probability schema, choice of, 81
- Procatactic causes of ill-health, 98 et seq.
- factors of ill-health explained, 26
- Prognosis, group and individual, difference between, 16
- Projectile factory, minor accidents in, cause of incidence of, 132
- Proteins, supply of, to keep human machine in repair, 99, 100
- Prussia, administrative districts, death-rate of tuberculosis, town and country compared, 355
- Psyche ( $\psi\psi\chi\eta$ ), primary meaning and other various meanings of, 127
- Psychological illness, end-results belonging to corporeal sphere, really manifestations of, 130
- Psychological procatactic factors, 127 et seq.
- Psychology—
- dynamic, of Freud, opposition to, 130
- study of, important to practical epidemiologists, 134
- Psycho-neurotic temperaments, symptoms of, high percentage discovered in victims of telegraphist's cramp, 131, 132
- Public health officers, controversy with biometricians, 64, 65
- Public schools, four great—
- influenza pandemic at (1918)—
- numbers attacked in summer and re-attacked in autumn, 86
- numbers not attacked in summer and attacked in autumn, 86
- Pulteney, Dr., 261
- Putrid fever. *See* Typhus fever
- Quantities, only great or small in relation to some other quantity in mathematical reasoning, 80
- Quarantine measures against cholera, of doubtful value, 72
- Queensland, smallpox in, first record of, 228
- Quetelet, L. A., pioneer in statistical methodology, 63
- Radwinter (Essex), diphtheria at (1876), 198
- Rain, effect of, on cholera, 170
- Rationing, administration of, difficulties besetting, 109
- Rations, individual, apportionment of, in prisons, result of, 103
- Rats—
- in relation to plague in East
- study of, in relation to plague, 307
- Reading—
- and Bolton, economics of, compared, 121
- Northampton, Bolton, Warrington, mortality - rates from all causes expressed in terms of Reading (1911-13), 120, 121
- Warrington, Northampton, Bolton, comparison of death-rates from all causes per 1,000 persons (1911-13), 120
- Rectum, cancer of, fatality of, generally distributed over all social classes, 369
- Registrar-General, decennial analysis of mortality in occupations, 123, 124
- Respiratory diseases, mortality-rate from, correlation with mean air-temperature in week before date of registration of death, 66
- Rhazes—
- excellence of natural history of smallpox given by, 29
- on danger of measles, 180
- Rokitansky, 351
- Roman Empire, occurrence of diphtheria in days of, 197

- Roman physicians, extent of knowledge of tuberculosis, 344
- Rome—  
Greek physicians at, character of, 25  
outbreak of bubonic plague at, during time of Galen, 25
- Ross, Sir Ronald, 54
- Royal Jennerian Institute, foundation of, 263
- Royal Naval School, Greenwich, distribution of immunity to diphtheria in a group, 208
- Rural and urban death-rates of tuberculosis, compared, 355
- Russia—  
capital cities of, outbreak of cholera in, in 1830-31, 166  
cholera in, 1907-9, statistics of deaths from, 168
- St. Pancras, measles in (1916-28), intensive study of, 192  
measles, epidemic of (1926), distribution among families, 185
- Santa Catharina (Brazil), epidemic of typhoid among German ranchers at, 159
- Santoro, Santorio, pioneer of quantitative study of nutrition, 98
- Scarlet fever—  
account of prevalence of, in middle of sixteenth century, 211  
affecting children mainly, 137  
and diphtheria, frequency of epidemics compared, 205  
and measles, mortality compared, 183  
and tuberculosis compared, 351  
changes of type of, 212, 223  
deadly form in last years of eighteenth century, 212  
death-rate, small at present time, 214, 216  
effect of isolation upon, 217-222  
effect of overcrowding upon, 220  
high mortality from, in 1863, statistics, 214  
history of, 211  
leading cause of death among infectious diseases of childhood from 1830 to 1875, 212, 213
- Scarlet fever (*cont.*)—  
measles, diphtheria, and whooping cough, death-rates in quinquennial periods under 15 years, 181  
mild form of, at present time, 216  
mild in early part of nineteenth century, 212  
mortality from, of children in Liverpool, 214  
mortality of diphtheria in Europe compared with that of, 197  
present decline in severity and mortality of, reason unknown, 65  
profound modification in type, 345  
Schick test of resistance to diphtheria, 205, 208
- Schönlein, 351
- Schools of different social classes, difference of evolution of diphtheria epidemics in, 208
- Scurvy—  
food-deficiency disease, 110  
outbreak of, among prisoners at Millbank Penitentiary following change for the worse in diet, 112
- Sedentary work, energy requirements of, tabulated, 104
- Sedentary worker, requirements of, under different conditions, results tabulated, 103
- Seguin and Lavoisier, demonstration that the consumption of oxygen increased as the amount of manual work done increased, 98, 99
- Self-sufficiency, intellectual, of Greeks of first century, 24, 25
- Sennart, 211
- Serbia, mortality from typhus in, during Great War, 177, 178
- Sewerage, defective, one probable cause of throat illness in Kilburn and St. John's Wood, 201-203
- Sexes, equalization in numbers of, how attained, 43

- Sexual act, performance of, over-estimation of by the herd, 341
- Shakespeare's *Macbeth* (quoted), 129
- Sheffield—  
 periodicity of measles in, 191  
 smallpox epidemic (1887-88)—  
   attacks and recoveries among vaccinated and unvaccinated compared, 283  
   proportion of recoveries among vaccinated and unvaccinated, 284
- Shell-shock, admission of medical importance of psychic factor in, 130
- Short, Thomas—  
 collation of Parish Registers by, 40  
*New Observations* of, important epidemiologically, 47
- Sickness, over-average, study of concomitants of, 49
- Siliceous particles, occupations entailing exposure to action of, setting up tuberculosis, 358, 359
- Simmonds. *See* McCollum and Simmonds
- Simon, Sir John, 245, 248  
 abilities contrasted with those of W. Farr, 54, 145, 146  
 campaign waged by, on filth and filthy water, in reduction of cases of typhoid fever, 157  
 characteristics of, 248  
 commendation of Budd's researches on typhoid, 144  
 conclusion as to origin of outbreak of typhoid at Windsor, 143  
 remarks on origin of typhoid fever through filth, 144  
 summing up of findings regarding epidemic of typhoid, at Terling (Essex), 55, 56  
 technique of, exhibited in epidemic of typhoid at Terling (Essex), 55
- Simpson, 297
- Sleeping-rooms in the country, over-crowding of, effect on tuberculosis mortality, 355
- Smallpox, 226-244  
 and measles, mortality from, compared in children in Glasgow, 182, 183  
 case of, vaccinated by Jenner ten years previously, 264  
 effect of cowpox on susceptibility to, 245  
 epidemic of 1825, fatality-rate of vaccinated and unvaccinated, 275  
 epidemic, 1838-39, mortality from, regularity of decline in, 53  
 epidemics of, 227  
   in particular towns, attacks and recoveries in vaccinated and unvaccinated compared, 283, 284  
 epidemiology of, 226  
 fatalities from, among vaccinated and unvaccinated, per cent, compared, tabulated returns, 285, 286  
 fatality from, results of dermal changes produced by vaccination on, 96, 97  
 in Australia, 228 et seq.  
 in Baltimore, 236  
   deaths from (1811-1920), table of, 232, 233  
 in Brazil, 242  
 in Britain, age distribution, variations in, 240  
 in England, 242  
   age incidence of, 227  
   first record of, 227  
 in London, 239  
 in New South Wales, 228  
   first record of, 228  
 in particular towns, table of, 283, 284  
 in Queensland, first record of, 228  
 in South Africa, 242  
 in Sweden, 227  
 in Sydney, 229  
   table showing distribution, 230  
 in Victoria, 231  
 inoculation in, epidemiological importance of, 226  
 international statistics in relation to vaccination, table of, 286  
 modification in type of, 345

- Smallpox** (*cont.*)—  
 natural history of, given by Rhazes, excellence of, 29  
 origin of, 227  
 prophylaxis of, by vaccination—  
     effect on fatality, 274, 275  
     table of, 276  
 fatality in relation to environment, 277  
 no straight control experiment in, 274  
 recent vaccination a defence against taking, 287  
 second attacks of, rare, 252  
 source of, 254  
 type of, epidemiologically considered, remains constant, 243  
*See also* Vaccination
- Smith, May**, demonstration of psychological differentiation of victims of telegraphist's cramp as a group, 131
- Social classes**—  
 Census, 1921—  
     mean ratio of registered to 100 calculated deaths, 124, 125  
     number of males aged 20-65, 125  
 five (males), mortality (standardized) from cancer of various sites, 368, 369  
     tabulated, 370, 371
- Social evils**—  
 described and denounced by those ignorant of the complexity of the problem, 126  
 method of description by Dickens criticized by Walter Bagehot, 126
- Socrates**, 268
- Soil contamination**—  
 alleged cause of prevalence of typhoid fever at Munich, 150  
 as secondary factor in origin of typhoid epidemic at Maidstone, 151
- Solitary confinement** one cause of death in prisoner suffering from mal-nutrition at Millbank Penitentiary, 112
- Somerville, Lord**, 257
- Soper, H. E.**, on periodicity of measles in Glasgow, 188, 189
- Soul**, first idea of, 127
- Soul-body**, study of, gradually becoming ignored by professional physicians, 129
- South Africa**, smallpox in, 242
- Standard "man"**—  
 calorie requirements of, investigations into, 107  
 each member of a family expressed as a fraction of a, 106
- State Health Department**, establishment of, 54
- State-supported families**, physiological circumstances of, need investigation, 108
- Statistic methodology**, pioneers in, 63
- Statistical argument** regarding vaccination against smallpox, 277-283  
 measure of infectiousness (1841), 185
- Statistical method**—  
 applied to data of human recorded experience, difficulty of finding "laws" of epidemic happenings through, 67  
 indispensable to work of epidemiologists, 17  
 lack of, principal cause of failure in advance of epidemiology, 21
- Statistical methodology**, upholders of, criticism of laboratory experiments by, 63, 64
- Statistics**—  
 definition of, 16  
 etymological meaning of, 15
- Stevenson, T. H. C.**—  
 highly preventable nature of large proportion of cancer mortality, 369  
 on diagnosis and mortality in respect of cancer in "accessible" and in "inaccessible" sites, 363  
 table illustrating death-rate from tuberculosis in London boroughs, diminishing according to wealth, increasing according to poverty, 356, 357, 358

Sticker, 171

on study of measures taken to control cholera (quoted), 72

on the progress of cholera (1817), 165, 166

Stockholm, percentage of infections of syphilis in, 339

Stocks, Percy, and Karn, Mary N., intensive study of history of measles in St. Pancras (1916-28), 192

Street hawker, sole occupation, showing poverty as primary factor in aetiology of tuberculosis, 358, 359

Stuart Period and beginning of nineteenth century, no great changes in mortality from phthisis during, 349

Suez Canal, opening of, fear of spread of cholera through, 167

Sunderland, quay of, cases of Indian and Asiatic cholera at, in 1831, 165

Sussex, death-rate from phthisis, 348  
*See also* England and Wales

Süssmilch, Johann Peter, 51

follower of Graunt's method in Germany, 43

Sweat, English. *See* English sweat

Sweden—

percentage of infections of syphilis in, 339

smallpox in, 227

and England, mortality-rates, male and female, ages 10-54 (1901-10), 117, 118, 119

Swine-fever, outbreaks of, extinction by slaughter, when only available, 71

Switzerland—

percentage of gonorrhoeal infection in, 340

percentage of infections of syphilis in, 339

Sydenham, Thomas, 17, 18, 21, 33, 46, 48, 49, 51, 138, 211, 227, 242

account of smallpox, 36

Bills of Mortality disregarded by, 41  
changes in epidemic diseases noted by, 36

Sydenham, Thomas (*cont.*)—

clinical convergence of "different" diseases to a common type, 37

clinical observations of patients recorded by, 35, 36

constitutions of, 178

epidemiological teaching of, 36, 37  
errors of, 35

"explanation" of hysterics by, 130

failure to use existing statistical data regarding mortality from disease, 39, 40

impartial estimate of his work, 38

Sydney, smallpox in, 229

Syphilis—

and diseases of syphilitic origin, standardized mortality from per 1,000,000 living, England and Wales (1911-28), 337, 338

and glossitis, as predisposing causes of cancer of the tongue, 369, 371

estimation of number of persons likely to acquire, 339

extreme severity of second stage of, in early times, 332

mortality from—

factor influencing, 338

in early times, 332

originator of word, 58

percentage of infections in Hamburg, Switzerland, and Sweden, 339

serious clinical manifestations of, in Elizabethan age, 331

Tabes dorsalis, mortality from, 337, 338

Tarbagan—

hunting of, resulting in Manchurian epidemic of plague, 308

local tradition relating to, 308

Tarring, West—

time- and space-distribution of typhoid fever cases (March-December 1893), 151, 152

typhoid fever epidemic at. *See* "Worthing"

- Telegraphist's cramp—  
 admission of medical importance  
 of psychic factor in, 130  
 history of opinion on, summarized,  
 131  
 investigation of Industrial Fatigue  
 Research Board into (1927),  
 131  
 victims of, high percentage of  
 symptoms of psycho-neurotic  
 temperament discovered in,  
 131, 132
- Temperament as a factor in determin-  
 ing ill-health, 26
- Temperature of factory, diminution  
 or over-excess of, frequency  
 of accidents corresponding  
 with, 132
- Tenement housing in Glasgow,  
 measles generated by, at  
 early age, 194
- Terling, Essex, typhoid epidemic at  
 (1867), Simon's comments  
 upon, 55, 56
- Thomas Aquinas, St., 131  
*Questiones disputatae de Anima*,  
 129
- Thomson, Theodore, presiding in-  
 spector at inquiry regarding  
 origin of Maidstone epi-  
 demic of typhoid fever, 149
- Thorne, W. Thorne, report on epi-  
 demic of typhoid at Terling  
 (Essex) (1867), 55
- Thorne-Thorne, R., Milroy Lecturer  
 on Diphtheria, 198
- Throat illness in Kilburn and St.  
 John's Wood, outbreak of,  
 epidemiological detection of,  
 201
- Tongue, cancer of—  
 greater prevalence in lowest social  
 classes, 369  
 improved surgical and radiological  
 treatment of, 372  
 non-specific predisposing causes,  
 369, 371
- Towns, "strain" and "pace of life" in,  
 122
- Townsmen, ageing, of insured class,  
 boredom attendant on life  
 of, 122, 123
- Traffic accidents—  
 constitute a crowd-disease, 377  
 more deadly than epidemic diseases,  
 377
- Transition, ages of, characterized by  
 individual and crowd emo-  
 tional reactions, 130
- Tripod of the Empirics, 24
- Tuberculosis, 342 et seq.  
 aetiology of, medical research into,  
 351  
 and dysentery, mortality from, in  
 mental hospitals compared,  
 343  
 antiquity as a crowd-sickness, 343,  
 344  
 as a specific infective disease, first  
 proof of, 351  
 compared with scarlet fever and  
 measles, 351  
 death-rate from, in London  
 boroughs, diminishing ac-  
 cording to wealth, increasing  
 according to poverty, table  
 illustrating, 356, 357, 358  
 death-rates, in administrative dis-  
 tricts of Prussia, town and  
 country compared, 355  
 decrease, coincident with present  
 deadliness of, 345  
 epidemic in mental hospitals of  
 England and Wales in last  
 years of Great War, 342,  
 343  
 excessive death-rate at Northamp-  
 ton (ages 15-25) largely due  
 to tuberculosis (footnote),  
 120  
 genesis of, three factors involved in,  
 359  
 incidence heavy upon shoe-makers  
 (footnote), 120  
 incidence in time without abrupt  
 variation, 342  
 increased prevalence in the future,  
 possible circumstances en-  
 tailing, 360  
 knowledge of, among physicians of  
 antiquity, 344  
 mortality—  
 a measure of poverty, 356, 357,  
 358

Tuberculosis (*cont.*)—mortality (*cont.*)—

effect of overcrowded sleeping-rooms in the country on, 355

fourteen groups of occupations with twice that of all occupied and retired males, 358, 359

frequently greater in rural districts, 355

in England and Wales, annually, 345

mortality-rate, decline in, reason still unknown, 65

prevalence in the printing industry, principal factors in causation, 359

## pulmonary—

death - rate, standardized, per 1,000,000 persons, in 1850 and in 1928, compared, 349

death-rates, comparative, at various ages, male and female (England and Wales, London, Bedfordshire, Lancashire, Sussex), 348

decline of, as observed and as would have been observed had the reduction followed a geometric rate of progress, 350

## mortality from—

decline in, hypotheses regarding explained, 349, 351, 352  
increasing during the Great War (1914-18), 349

statistical evidence discussed, 354, 355

open-air treatment advocated by Pliny the Elder, 344, 345

segregation of "open" cases, 354  
unity as a pathological process, first demonstration of, 351

virus of, first isolated by Koch, 351

Turner, on results of dermal changes produced by vaccination on smallpox fatality, 97

## Typhoid fever—

## and typhus fever—

criterion of likeness or difference, biological, 138

Typhoid fever (*cont.*)—and typhus fever (*cont.*)—

group difference between, known to Sir William Jenner, 139, 140

original confusion between, 138  
when first differentiated, 139

## at Munich—

causation, 158, 159

deaths from (1851-73), 149

prevalence of, alleged cause, 150  
average number of men in 17th Lancers protected by previous attack, 92

death-rates (standardized) at all ages (1870-1931), England and Wales, tabulated, 156, 157  
deaths from, in Munich (1851-1906), 149

England and Wales (1871-1931), effect on prevalence of gradual purification of water supplies, 158

## epidemic—

at Bolton-upon-Deane (1921), 56, 160

due to polluted water supply, 161, 162

at Maidstone (1897), 146

course taken by, 17

soil contamination as secondary factor in origin of, 151

water-borne origin of, arguments against, 148

water-borne origin of, discussed, 147, 148, 149, 151, 156, 159, 162

weekly table of attacks and notifications, with totals, 147

at Malton (1932), due to polluted water supply, 162

at Santa Catharina (Brazil), 159

at Terling (Essex) (1867), Simon's comments on, 55, 56

at Viaductos, Brazil, 159

at "Worthing," "West Worthing," West Tarring, and Broadwater (1893), 152 et seq.

number of attacks ascertained to have commenced in each fortnight (March-December

- Typhoid fever (cont.)—**  
 epidemic (cont.)—  
   at "Worthing," etc. (cont.)—  
     number of cases notified in each  
     locality fortnightly (March–  
     December 1893), 151  
     question of origin in water  
     supply discussed, 154, 155,  
     156  
     time- and space-distribution of  
     cases in the several localities,  
     151, 152  
 incidence upon the 17th Lancers,  
 Meerut (1905–9), 90, 91, 92,  
 93, 94  
 infection from the *materies morbi*,  
 140  
 outbreak at Windsor, aetiology of,  
 143, 144  
 prevalence due to pollution of water  
 supply and that due to  
 carrier infection, characters  
 contrasted, 17  
 prevalent in France, but rare in  
 England, at end of eighteenth  
 century, 139  
 propagation by "filth," belief in, 144  
 protection against. *See* Anti-typhoid  
 inoculation  
 standpoint of physicians and epi-  
 demiologists with regard to,  
 contrasted, 15  
 time-chart of cases, diagnostic value  
 of, 17  
 transmission by "carriers," 158  
 water-borne, 146 et seq., 161
- Typhoid group—**  
 epidemiology of, achievements illus-  
 trating, 62  
 of illnesses, 137 et seq.
- Typhus fever—**  
 and social misery, connection be-  
 tween, example of, 175  
 and typhoid—  
   criterion of likeness or difference,  
   biological, 138  
   original confusion between, 138  
   when first differentiated, 139  
 causes of, 178, 179  
 controllability of, 179  
 death-rate from, in British Isles and  
 Germany 50 years ago, 173
- Typhus fever (cont.)—**  
 disappearance of, 345  
 in England in early nineteenth  
 century, 178  
 in French army during retreat  
 from Moscow, 177  
 mortality from, in Serbia during  
 Great War, 177, 178  
 origin of, general former belief as  
 to, 140  
 outbreak of—  
   in European Wars, examples of,  
   176, 177  
   in Kidderminster (1756), 178  
 special example of pestilence,  
 137  
 statistics of—  
   in Eastern Europe, 173  
   in Western Europe, 173
- Under-rationing in prisons, how pro-  
 duced, 103**
- Uninoculated and inoculated, attack-  
 rates upon, compared, 83,  
 84, 85**
- United States of America, cancer  
 mortality, "accessible" and  
 "inaccessible" sites com-  
 pared, 363**
- Unvaccinated, fatality of, per cent,  
 from smallpox, observed,  
 tabulated returns showing,  
 285, 286**
- Uppingham and Broadstairs, schools  
 at, differential preventive  
 treatment of acute polio-  
 myelitis, 313, 314**
- Urban and rural death-rates of tuber-  
 culosis compared, 355**
- Uterus, cancer of, death-rate from,  
 of single women much lower  
 than that of married women,  
 374**
- Vaccinated, the, fatality of, per cent,  
 from smallpox observed and  
 calculated, tabulated returns  
 showing, 285, 286**

- Vaccination**—  
 author's views on, 243  
 controversy regarding, 78, 243, 277 et seq.  
 Jenner and Creighton, 245 et seq.  
 effect on modification of age distribution, 241  
 in Australia, 228  
 statistical argument regarding, 277-283
- Vaccinations**—  
 in New South Wales (1871-80), 228  
 in Victoria (1874-84), 228  
 and vaccination-rates in Baltimore (1827-1918), table of, 232, 233  
 recent, a defence against taking smallpox, 287
- Vaccine Board**, formation of, 263
- Varicella**, prevalence of, in Australia, 231
- Variolae vaccinae**, Creighton's denunciation of term, 269, 270
- Venereal diseases**—  
 disastrous mismanagement of, 333  
 epidemic nature of, at beginning of sixteenth century, 331  
 failure in prevention of, causes, 333, 334  
 incidence upon inoculated and uninoculated examined, 95, 96  
 increase of, due to barbarism, coincident with the Great War (1914-18), 340  
 moral stigma in prophylaxis of, 334  
 prevalences of, 331  
 epidemiological significance, 340  
 preventibility of, 341
- Vernon, H. M., and Osborne, Ethel**, cause of incidence of minor accidents in a projectile factory, 132
- Vesalius, 25**
- Viaductos (Brazil)**, epidemic of typhoid among Brazil-born Italians at, 159
- Vibrios (cholera)**, length of time of survival of, question of, 171
- Victoria**, smallpox in, history of, 231
- Villemin**, proof by, that tuberculosis is a specific infective disease, 351
- Vital animal and vegetable spirits**, doctrine of, 22
- Vital statistics**—  
 first demonstrator of, facts of, 43  
 system of, prerequisite in medical research, 46
- Vitamins**—  
 diet rich in, doubt as to control of herd-illness by, 77  
 over-estimation of importance attaching to, 115  
 popular interest taken in, 110
- Wallace, A. Russel**, 251
- Walthamstow**, paratyphoid outbreak at (1931), due to infected milk, 163
- Wanklyn, Dr.**, on depression of industrial town life (quoted), 123
- Warrington**—  
 smallpox epidemic (1891-92)—  
 attacks and recoveries among vaccinated and unvaccinated compared, 283  
 proportion of recoveries among vaccinated and unvaccinated, 284
- Bolton, Northampton, Reading**, comparison of death-rates from all causes per 1,000 persons (1911-13), 120
- Reading, Northampton, Bolton**, mortality-rates expressed in terms of Reading (1911-13), 120, 121
- Wars, European**, outbreak of typhus in, examples of, 176, 177
- Water-borne origin**, examples of typhoid epidemics not of, 159
- Water supply**, polluted—  
 cause of epidemic of typhoid fever, Bolton-upon-Deane, 161, 162  
 character of typhoid prevalence due to, 17  
 question discussed of causation by, of typhoid epidemic—  
 at Maidstone (1897), 147, 148, 149, 151, 156, 159, 162  
 at "Worthing," "West Worthing," West Tarring, and Broadwater (1893), 154, 155, 156

Water supplies—

communal, gradual purification of,  
effect on diminution of  
typhoid fever in England and  
Wales (1871-1931), 158

contamination of, cholera kept alive  
by, 169

Watt, Robert, comparison of mor-  
tality from smallpox and  
measles in Glasgow (1783-  
1812), 182

Weather—

in relation to prevalence of disease,  
observations of Hippocrates  
upon, 23

relation of, to *Katastasis* of Hippo-  
crates, 20, 21

Webster, Dr., effect of breeding from  
stocks found to be resistant  
to specific infection on epi-  
demic herd-sickness, 76, 77

Were-wolves. *See* Lycanthropy

West European States, decline in  
mortality from phthisis, 349

Westmorland, mortality rates from  
pneumonia and bronchitis,  
male and female, ages 45-55,  
55-65 (1901-10), 119, 120

White, Gilbert—

on cuckoo's egg, 250

on leprosy, 254, 255

Whooping cough, measles, scarlet  
fever, diphtheria, death-  
rates in quinquennial periods  
under 15 years, 181

Willan, on prevalence of scarlatina  
(1798), 212

Willcox, Dr. (Cornell University), on  
causes of increase in cancer  
mortality, 361, 363

Windsor, outbreak of typhoid fever at,  
aetiology of, 143, 144

Wintrincham (the elder), 48

Women, cancer mortality among,  
variability in course of, 373

Woods, H. M., effect of isolation on  
scarlet fever, 216 et seq.

Woodville, W., 257, 258

report on cowpox inoculation, 258

Woolcombe, William—

revival in medical statistics ex-  
hibited by monograph of, 49

Woolcombe, William (*cont.*)—

*The Frequency and Fatality of  
Different Diseases, Particu-  
larly of the Progressive In-  
crease of Consumption* (1808)  
(quoted), 345, 346, 347

Work performed, heat production in  
relation to, experiments tabu-  
lated, 100, 101

"Worthing"—

time- and space-distribution of  
typhoid fever cases (March-  
December 1893), 151, 152

"West Worthing," West Tarring,  
and Broadwater—

typhoid epidemic at (1893), 152  
et seq.

number of attacks ascertained  
to have commenced in each  
fortnight (March-December  
1893), 153

number of cases notified fort-  
nightly (March-December  
1893), 151, 152

question of origin in water  
supply discussed, 154, 155,  
156

"West"—

time- and space-distribution of  
typhoid fever cases (March-  
December 1893), 151, 152

typhoid fever epidemic at. *See*  
"Worthing"

Writing, clearness of, a requisite in  
describing epidemiological  
phenomena, 62

Württemberg, immense reduction of  
population through typhus  
in Thirty Years War, 176

Young members of town crowd  
fuller and more interesting  
life than that of young  
countrymen, 122

Yule, Udny—

*Introduction to the Theory of  
Statistics* (quoted), 82

and Greenwood, M., on results of  
anti-cholera inoculation in  
Greek Sanitary Corps, 96



















